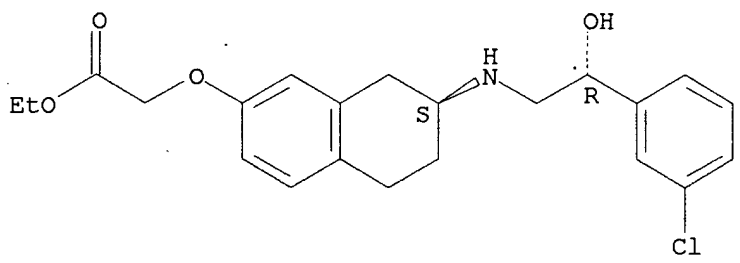
L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 121524-09-2 REGISTRY
CN Acetic acid, [[(7S)-7-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetic acid, [[7-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]-5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester, hydrochloride, [R-(R*,S*)]-
OTHER NAMES:
CN **SR 58611**
CN SR 58611A
FS STEREOSEARCH
MF C22 H26 Cl N O4 . Cl H
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, MEDLINE, PHAR, PROMT, TOXCENTER, USPATFULL
CRN (121524-08-1)

Absolute stereochemistry.



● HCl

51 REFERENCES IN FILE CA (1962 TO DATE)
52 REFERENCES IN FILE CAPLUS (1962 TO DATE)

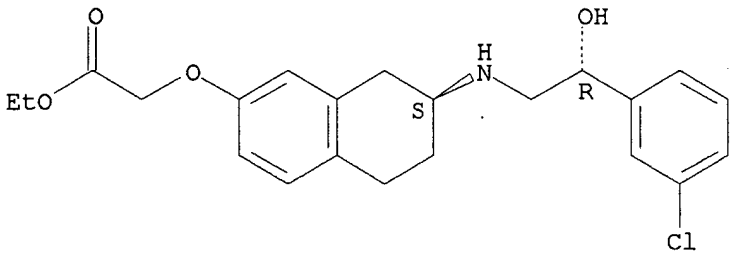
=> s (sr 58611a)/cn
L4 1 (SR 58611A)/CN

=> d l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 121524-09-2 REGISTRY
CN Acetic acid, [[(7S)-7-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetic acid, [[7-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]-5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester, hydrochloride, [R-(R*,S*)]-
OTHER NAMES:
CN SR 58611
CN **SR 58611A**
FS STEREOSEARCH

MF C22 H26 Cl N O4 . Cl H
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, MEDLINE, PHAR, PROMT, TOXCENTER, USPATFULL
CRN (121524-08-1)

Absolute stereochemistry.



● HCl

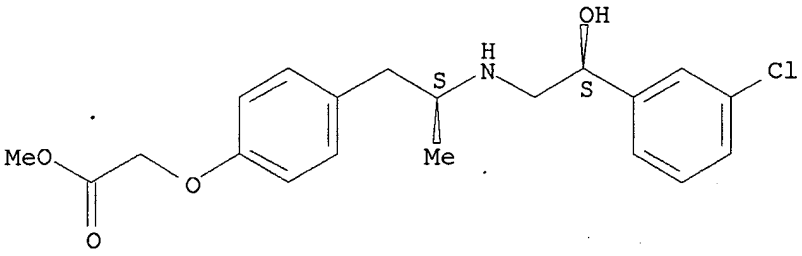
51 REFERENCES IN FILE CA (1962 TO DATE)
52 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> s (brl 35135)/cn
L5 1 (BRL 35135)/CN

=> d l5

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 86615-96-5 REGISTRY
CN Acetic acid, [4-[(2R)-2-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]phenoxy]-, methyl ester, rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetic acid, [4-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]phenoxy]-, methyl ester, (R*,R*)-(.+-.)-
OTHER NAMES:
CN Acetic acid, [4-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]phenoxy]-, methyl ester, (R*,R*)-
CN **BRL 35135**
FS STEREOSEARCH
DR 78069-22-4
MF C20 H24 Cl N O4
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, DRUGNL, DRUGUPDATES, IPA, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

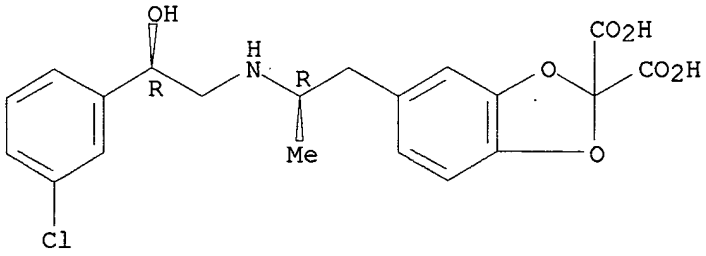
42 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
42 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> s (cl 316243)/cn
L6 1 (CL 316243)/CN

=> d l6

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 138908-40-4 REGISTRY
CN 1,3-Benzodioxole-2,2-dicarboxylic acid, 5-[(2R)-2-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-, disodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,3-Benzodioxole-2,2-dicarboxylic acid, 5-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-, disodium salt, [R-(R*,R*)]-
OTHER NAMES:
CN **CL 316243**
CN HP 186
FS STEREOSEARCH
DR 151126-84-0
MF C20 H20 Cl N O7 . 2 Na
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, DRUGNL, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
CRN (183720-02-7)

Absolute stereochemistry.



●2 Na

118 REFERENCES IN FILE CA (1962 TO DATE)
118 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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=> s (az 002)/cn
L7            0 (AZ 002)/CN

=> s (az002)/cn
L8            0 (AZ002)/CN

=> s (bms 187257)/cn
L9            1 (BMS 187257)/CN

=> d l9

L9   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   182967-43-7  REGISTRY
CN   5-Thiazolebutanoic acid, 2-[(2S)-2-[[(2R)-2-hydroxy-3-
     phenoxypropyl]amino]propyl]-, rel- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   5-Thiazolebutanoic acid, 2-[2-[(2-hydroxy-3-phenoxypropyl)amino]propyl]-,
     (R*,S*)-
OTHER NAMES:
CN   BMS 187257
FS   STEREOSEARCH
MF   C19 H26 N2 O4 S
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS

Relative stereochemistry.
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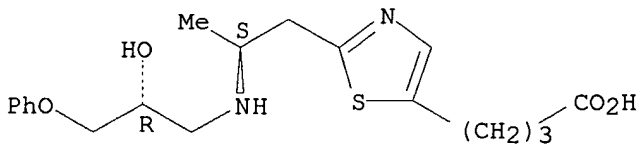

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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=> s (zd 7114)/cn
L10           1 (ZD 7114)/CN

=> d l10

L10  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   129689-30-1  REGISTRY
CN   Acetamide,
2-[4-[2-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]ethoxy]phenoxy]-
     N-(2-methoxyethyl)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Acetamide,
2-[4-[2-[(2-hydroxy-3-phenoxypropyl)amino]ethoxy]phenoxy]-N-(2-
     methoxyethyl)-, (S)-
OTHER NAMES:
CN   ICI-D 7114
CN   ZD 7114
CN   Zeneca ZD 7114
FS   STEREOSEARCH
MF   C22 H30 N2 O6
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS,
       CSCHEM, DRUGNL, DRUGUPDATES, EMBASE, MEDLINE, PHAR, RTECS*, TOXCENTER,
       USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
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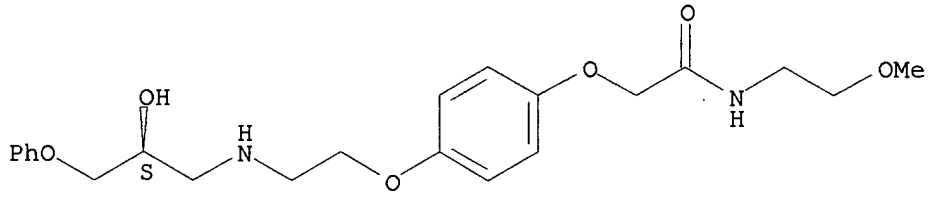


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             35 REFERENCES IN FILE CA (1962 TO DATE)
             35 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> s (ro 402148)/cn
L11           0 (RO 402148)/CN

=>
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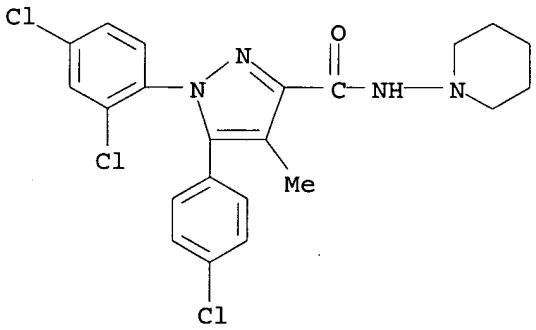
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 168273-06-1 REGISTRY
CN 1H-Pyrazole-3-carboxamide, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-N-1-piperidinyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Rimonabant
CN **SR 141716**
FS 3D CONCORD
MF C22 H21 Cl3 N4 O
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, CASREACT, CIN, DRUGNL, DRUGPAT, DRUGUPDATES, PROMT, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

65 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
65 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=>

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1614jmk

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	May 29	PASCAL enhanced with additional data

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 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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FILE 'HOME' ENTERED AT 10:46:24 ON 30 MAY 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:46:35 ON 30 MAY 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 MAY 2003  HIGHEST RN 521913-14-4
DICTIONARY FILE UPDATES:  28 MAY 2003  HIGHEST RN 521913-14-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s (sr 141716)/cn
L1            1 (SR 141716)/CN

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   168273-06-1  REGISTRY
CN   1H-Pyrazole-3-carboxamide, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-
     methyl-N-1-piperidinyl- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Rimonabant
CN   SR 141716
FS   3D CONCORD
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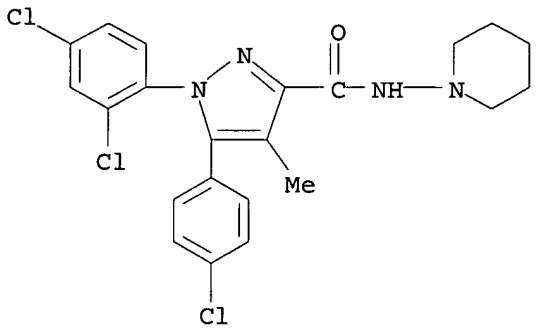
MF C22 H21 Cl3 N4 O
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, CASREACT, CIN, DRUGNL,
    DRUGPAT, DRUGUPDATES, PROMT, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

65 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
65 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.30	6.51

FILE 'STNGUIDE' ENTERED AT 10:46:56 ON 30 MAY 2003
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 23, 2003 (20030523/UP).

=> file uspatful

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	6.57

FILE 'USPATFULL' ENTERED AT 10:47:15 ON 30 MAY 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 29 May 2003 (20030529/PD)
FILE LAST UPDATED: 29 May 2003 (20030529/ED)
HIGHEST GRANTED PATENT NUMBER: US6571393
HIGHEST APPLICATION PUBLICATION NUMBER: US2003101500
CA INDEXING IS CURRENT THROUGH 29 May 2003 (20030529/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 29 May 2003 (20030529/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<

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>>>  published document but also a list of any subsequent                <<<
>>>  publications.  The publication number, patent kind code, and        <<<
>>>  publication date for all the US publications for an invention       <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL     <<<
>>>  records and may be searched in standard search fields, e.g., /PN,   <<<
>>>  /PK, etc.                                                           <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together          <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to            <<<
>>>  enter this cluster.                                                 <<<
>>>                                                                      <<<
>>>  Use USPATALL when searching terms such as patent assignees,         <<<
>>>  classifications, or claims, that may potentially change from       <<<
>>>  the earliest to the latest publication.                             <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s 5624941/pn
L2            0 5624941/PN

=> s us5624941/pn
L3            1 US5624941/PN

=> d his

     (FILE 'HOME' ENTERED AT 10:46:24 ON 30 MAY 2003)

     FILE 'REGISTRY' ENTERED AT 10:46:35 ON 30 MAY 2003
L1             1 S (SR 141716)/CN

     FILE 'STNGUIDE' ENTERED AT 10:46:56 ON 30 MAY 2003

     FILE 'USPATFULL' ENTERED AT 10:47:15 ON 30 MAY 2003
L2             0 S 5624941/PN
L3             1 S US5624941/PN

=> s l3 and l1
            11 L1
L4             1 L3 AND L1

=> d l4 kwic,hitstr

L4   ANSWER 1 OF 1  USPATFULL
PI     US 5624941              19970429                                <--
IT  168273-06-1P
       (prepn. of diarylpyrazoles as cannabinoid receptor agonists)
IT  168273-06-1P
       (prepn. of diarylpyrazoles as cannabinoid receptor agonists)
RN   168273-06-1  USPATFULL
CN   1H-Pyrazole-3-carboxamide, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-
       methyl-N-1-piperidinyl- (9CI)  (CA INDEX NAME)
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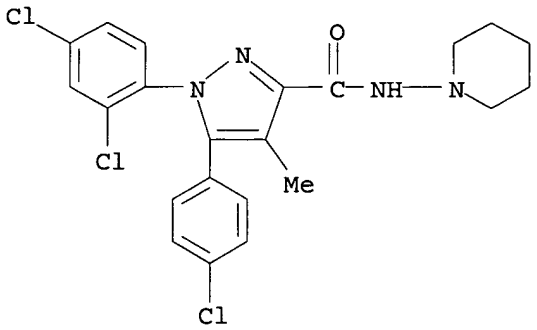


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=> d l4 full,hitstr,thru
'FULL' IS NOT A VALID FORMAT FOR FILE 'USPATFULL'
'THRU' IS NOT A VALID FORMAT FOR FILE 'USPATFULL'

The following are valid formats:

The default display format is STD.

ABS -------- AB
ALL -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,
             RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,
             DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,
             INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
             EXF, ARTU
ALLG ------- ALL plus PAGE.DRAW
BIB -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD, RLI,
             PRAI, DT, FS, EXNAM, LREP, CLMN, ECL, DRWN, LN.CNT
BIB.EX ----- BIB for original and latest publication
BIBG ------- BIB plus PAGE.DRAW
BROWSE ----- See "HELP BROWSE" or "HELP DISPLAY BROWSE".  BROWSE must
             entered on the same line as DISPLAY, e.g., D BROWSE.
CAS -------- OS, CC, SX, ST, IT
CBIB ------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PRAI, DT, FS
DALL ------- ALL, delimited for post-processing
FP --------- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI, RLI,
             PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL,
             NCLM, NCLS, EXF, REP, REN, ARTU, EXNAM, LREP,
             CLMN, DRWN, AB
FP.EX ------ FP for original and latest publication
FPALL ------ PI, TI, IN, INA, PA, PAA, PAT, PETRM, DCD, AI,
             RLI, PRAI, IC, ICM, ICS, INCL, INCLM, INCLS, NCL, NCLM,
             NCLS, EXF, REP, REN,ARTU, EXNAM, LREP, CLMN, DRWN, AB,
             PARN, SUMM, DRWD, DETD, CLM
FPBIB ------ PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI,
             RLI, PRAI, REP, REN, EXNAM, LREP, CLM, CLMN, DRWN
FHITSTR ---- HIT RN, its text modification, its CA index name, and
             its structure diagram
FPG -------- FP plus PAGE.DRAW
GI --------- PN and page image numbers
HIT -------- All fields containing hit terms
HITRN ------ HIT RN and its text modification
HITSTR ----- HIT RN, its text modification, its CA index name, and
             its structure diagram
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IALLG ------ IALL plus PAGE.DRAW
IBIB ------- BIB, indented with text labels
IBIB.EX ---- IBIB for original and latest publication
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IBIBG ------ IBIB plus PAGE.DRAW
IMAX ------- MAX, indented with text labels
IMAX.EX ---- IMAX for original and latest publication
IND -------- INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
             EXF, ARTU, OS, CC, SX, ST, IT
ISTD ------- STD, indented with text labels
KWIC ------- All hit terms plus 20 words on either side
MAX -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, PTERM, DCD,
             RLI, PRAI, DT, FS, REP, REN, EXNAM, LREP, CLMN, ECL,
             DRWN, AB, GOVI, PARN, SUMM, DRWD, DETD, CLM, INCL,
             INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
             EXF, ARTU OS, CC, SX, ST, IT
MAX.EX ----- MAX for original and latest publication
OCC -------- List of display fields containing hit terms
SBIB ------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,
             DT, FS, LN.CNT
SCAN ------- AN, TI, NCL, NCLM, NCLS, IC, ICM, ICS (random display
             without answer number.  SCAN must be entered on the
             same line as DISPLAY, e.g., D SCAN)
STD -------- AN, TI, IN, INA, PA, PAA, PAT, PI, AI, RLI, PRAI,
             DT, FS, LN.CNT, INCL, INCLM, INCLS, NCL, NCLM, NCLS,
             IC, ICM, ICS, EXF (STD is the default)
STD.EX ----- STD for original and latest publication
TRIAL ------ AN, TI, INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC,
             ICM, ICS

ENTER DISPLAY FORMAT (STD):all

L4   ANSWER 1 OF 1  USPATFULL
AN     97:36201  USPATFULL
TI     Pyrazole derivatives, method of preparing them and pharmaceutical
       compositions in which they are present
IN     Barth, Francis, Montpellier, France
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PI     US 5624941              19970429                              <--
AI     US 1994-348881          19941129 (8)
RLI    Continuation-in-part of Ser. No. US 1993-168237, filed on 17 Dec 1993,
       now abandoned which is a continuation-in-part of Ser. No. US 1993-79870,
       filed on 23 Jun 1993, now abandoned
PRAI   FR 1992-7645        19920623
       FR 1993-14444       19931202
       FR 1994-8974        19940720
DT     Utility
FS     Granted
REP    US 3449350       Jun 1969  546/275.400   Walker
       US 4826868       May 1989  514/407.000   Wachter et al.
       US 5013837       May 1991  544/143.000   Ward et al.
       US 5051518       Sep 1991  548/375.100   Murray et al.
       US 5134142       Jul 1992  514/255.000   Matsuo et al.
       US 5164381       Nov 1992  514/085.000   Wachter et al.
       EP 29363         May 1981
       EP 248594        Dec 1987
       EP 293220        Nov 1988
       EP 418845        Mar 1991
       EP 445781        Sep 1991
       EP 477049        Mar 1992
       EP 576357        Dec 1993
REN    Boyd et al., Journal of the Chemical Society, Perkin Transactions 1,
       vol. 21, 1973, pp. 2532-2535.
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Fusco et al., Tetrahedron Letters, No. 46, 1967, pp. 4541-4544.
CA110:75489 (Feb. 1989).

EXNAM Primary Examiner: Burn, Brian M.

LREP Bacon & Thomas

CLMN Number of Claims: 30

ECL Exemplary Claim: 1

DRWN No Drawings

AB The present invention relates to compounds of the formula: ##STR1## These compounds are useful in pharmaceuticals in which cannabis is known to be involved.

PARN The present application is a continuation-in-part application of U.S. Ser. No. 08/168,237, filed Dec. 17, 1993, now abandoned, which is a continuation-in-part application of U.S. Ser. No. 08/079,870, filed Jun. 23, 1993, now abandoned.

SUMM The present invention relates to novel pyrazole derivatives, to a method of preparing them and to the pharmaceutical compositions in which they are present.

Numerous pyrazole derivatives have been described in the literature; more particularly, EP-A-268554 and DE-A-3910248 claim pyrazoles possessing herbicidal properties, EP-A-430186 and JP-A-03031840 claim compounds useful for photography, and EP-A-418845 claims pyrazoles possessing antiinflammatory, analgesic and antithrombotic activity.

It has now been found that the pyrazoles forming the subject of the invention have a good affinity for the cannabinoid receptor and are therefore particularly valuable in the therapeutic areas in which cannabis is known to be involved.

.DELTA..sup.9 -Tetrahydrocannabinol, or .DELTA..sup.9 -THC, is the main active constituent extracted from Cannabis sativa (Tuner, 1985; In Marijuana 84, Ed. Harvey, D. Y., IRL Press, Oxford).

The effects of cannabinoids are due to an interaction with specific high-affinity receptors present in the central nervous system (Devane et al., Molecular Pharmacology, 1988, 34, 605-613) and peripheral nervous system (Nye et al., The Journal of Pharmacology and Experimental Therapeutics, 1985, 234, 784-791; Kaminski et al., 1992, Molecular Pharmacology, 42, 736-742; Munro et al., Nature, 1993, 365, 61-65).

Characterization of this receptor has been made possible by the development of specific synthetic ligands such as the agonists WIN 55212-2 (J. Pharmacol. Exp. Ther., 1993, 264, 1352-1363) or CP 55,940 (J. Pharmacol. Exp. Ther., 1988, 247, 1046-1051).

The therapeutic indications of cannabinoids pertain to a variety of areas such as the immune system, the central nervous system and the cardiovascular or endocrine system (Hollister, Pharmacological Reviews, 1986, 38, 1-20, Renv and Sinha, Progress in Drug Research, 1991, 36, 71-114, Cannabinoid receptor expression in human leucocytes, European Journal of Biochemistry, 1993, 214, 173-180.

More particularly, compounds possessing an affinity for the cannabinoid receptor are useful as lmmunomodulators and psychotropic agents, in thymic disorders, vomiting, myorelaxation, various types of neuropathy, memory disorders, dyskinesia, migraine, asthma, epilepsy and glaucoma or else in anticancer chemotherapy, in ischemia and angor, in orthostatic hypotension and in cardiac insufficiency.

Thus, according to one of its features, the present invention relates to the compounds of the formula ##STR2## in which

g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 are identical or different and are independently hydrogen, a chlorine or bromine atom, a (C.sub.1 -C.sub.3)-alkyl, a (C.sub.1 -C.sub.3)alkoxy, a trifluoromethyi or a nitro group and g.sub.4 is optionally a phenyl group;

R.sub.4 is hydrogen or a (C.sub.1 -C.sub.3)-alkyl;

X is either a direct bond or a group --(CH.sub.2).sub.x N(R.sub.3)--, in which R.sub.3 is hydrogen or a (C.sub.1 -C.sub.3)-alkyl and x is zero or one; and

R is

a group --NR.sub.1 R.sub.2 in which R.sub.1 and R.sub.2 are independently a (C.sub.1 -C.sub.6)-alkyl; an optionally-substituted non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical; an amino (C.sub.1 -C.sub.4) alkyl group in which the amino is optionally disubstituted by a (C.sub.1 -C.sub.3)-alkyl; a cycloalkyl-(C.sub.1 -C.sub.3) alkyl in which the cycloalkyl is C.sub.3 -C.sub.12 ; a phenyl which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C.sub.1 -C.sub.5)-alkyl or by a (C.sub.1 -C.sub.5)-alkoxy; a phenyl (C.sub.1 -C.sub.3)-alkyl; a diphenyl-(C.sub.1 -C.sub.3)-alkyl; a naphthyl; an anthracenyl; a saturated 5- to 8-membered heterocyclic radical which is unsubstituted or substituted by a (C.sub.1 -C.sub.3)-alkyl, by a hydroxyl or by a benzyl group; a 1-adamantylmethyl; an aromatic heterocycle unsubstituted or mono-or-polysubstituted by a halogen, a (C.sub.1 -C.sub.5)alkyl, a (C.sub.1 -C.sub.5)-alkoxy; a (C.sub.1 -C.sub.3)-alkyl substituted by an aromatic heterocycle unsubstituted or mono- or -polysubstituted by a halogen, a (C.sub.1 -C.sub.5) alkyl, a (C.sub.1 -C.sub.5)-alkoxy, or else R.sub.1 is hydrogen and R.sub.2 is as defined above, or else R.sub.1 and R.sub.2, together with the nitrogen atom to which they are bonded, form a saturated 5- to 8-membered heterocyclic radical, said heterocyclic radical being other than morpholine when w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 are all hydrogen;

a group R.sub.2 as defined above when X is --(CH.sub.2).sub.x N(R.sub.3)--; or

a group R.sub.5 when X is a direct bond, R.sub.5 being a (C.sub.1 -C.sub.3)-alkyl; a (C.sub.3 -C.sub.12)-cycloalkyl which is unsubstituted or substituted by a (C.sub.1 -C.sub.5)-alkyl; a phenyl-(C.sub.1 -C.sub.3)-alkyl which is unsubstituted or substituted by a halogen or by a (C.sub.1 -C.sub.5)-alkyl; a cycloalkyl-(C.sub.1 -C.sub.3)-alkyl in which the cycloalkyl is C.sub.3 -C.sub.12 and is unsubstituted or substituted by a (C.sub.1 -C.sub.5)-alkyl; or a 2-norbornylmethyl; or one of their salts, where appropriate.

The non-aromatic C.sub.3 -C.sub.15 carbocyclic radicals include saturated or unsaturated, fused or bridged monocyclic or polycyclic radicals, optionally terpene radicals. These radicals are optionally mono- or polysubstituted, said substiituent(s) being different from a substituted carbonyl group. Advantageously, the monocyclic radicals are substituted by at least one group selected among the (C.sub.1 -C.sub.5) alkyl, (C.sub.1 -C.sub.5)alkoxy, halogen or hydroxy groups, it being understood that in the case of terpenes or terpene radicals, for example bornyl, menthyl or menthenyl, the alkyl groups of the terpene are not considered as substituents.

The monocyclic radicals include cycloalkyls, for example cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl and cyclododecyl, which are unsubstituted or substituted by at least one (C.sub.1

-C.sub.5)-alkyl, (C.sub.1 -C.sub.5)-alkoxy, halogen or hydroxy groups.

The fused, bridged or spiranic dicyclic or tricyclic radicals include for example norbornyl, bornyl, isobornyl, noradamantyl, adamantyl and spiro[5,5]undecanyl, said radicals being unsubstituted or substituted by a (C.sub.1 -C.sub.5)-alkyl.

Saturated 5- to 8-membered heterocyclic radical is understood as meaning a fused or bridged, non-aromatic monocyclic, dicyclic or tricyclic heterocyclic radical, the heteroatom being S, O or N, or a non-aromatic monocyclic heterocyclic radical containing a nitrogen atom and an oxygen or sulfur atom, said radicals being for example tetrahydrofuranyl, tetrahydrothiofuranyl, tropyl, morpholinyl, thiomorpholinyl, piperidinyl, piperazinyl, pyrrolidinyl or quinuclidinyl, the 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, 4-morpholinyl and 4-thiomorpholinyl radicals being advantageous.

The aromatic heterocycles can be monocyclic or dicyclic, for example pyrrolyl, pyridyl, indolyl, quinolinyl, thiazolyl or isoindazolyl, these aromatic heterocycles being unsubstituted or substituted for example by halogens, (C.sub.1 -C.sub.5)-alkyl or (C.sub.1 -C.sub.5)-alkoxy. The prefered aromatic heterocycles are pyridyl, pyrrole, indole groups, the radicals 2-indolyl or 3-indolyl are particularly prefered.

In formula (I) above, preferably at least one of the substituents w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 is other than hydrogen.

In formula (I) above, when R is a Group --NR.sub.1 R.sub.2, preferably:

R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl group and R.sub.2 is as defined above for (I); or

R.sub.1 and R.sub.2 are each a (C.sub.1 -C.sub.6)-alkyl group or a (C.sub.3 -C.sub.6)-cycloalkyl group; or

R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl group and R.sub.2 is a cycloalkyl-(C.sub.1 -C.sub.3)-alkyl group in which the cycloalkyl is C.sub.3 -C.sub.12 ; a non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical which is unsubstituted or substituted as above mentioned; a phenyl which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C.sub.1 -C.sub.3)-alkyl or by a (C.sub.1 -C.sub.3)-alkoxy; a phenyl-(C.sub.1 -C.sub.3)-alkyl or a (C.sub.1 -C.sub.3)alkyl substituted by a 2- or 3-indolyl.

Particularly preferably, when R in formula (I) is a group --NR.sub.1 R.sub.2, R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl and R.sub.2 is a non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical, a cycloalkyl-(C.sub.1 -C.sub.3)-alkyl in which the cycloalkyl is C.sub.3 -C.sub.6, or a 2- or 3-indolyl-(C.sub.1 -C.sub.3)-alkyl.

The preferred alkyl groups are methyl, ethyl, propyl and isopropyl.

In formula (I) above, R is advantageously a group --NR.sub.1 R.sub.2 preferably selected from the radicals (1) to (74) below.

When R.sub.1 and R.sub.2, with the nitrogen atom to which they are bonded, are a heterocyclic, radical, this is preferably a 5-, 6- or 7-membered saturated heterocycle and can contain another heteroatom, especially oxygen or sulfur, for example a pyrrolidine, a piperidine, a hexahydroazepine, a morpholine or a thiomorpholine, with the limitation specified above.

The radicals represented by R as defined for (I) are preferably radicals

selected from:

(1) propylamino

(2) butylamino

(3) isopropylamino

(4) dipentylamino

(5) 2-(N,N-diethylamino)ethylamino

(6) benzylamino

(7) 2-phenylethylamino

(8) 3-phenylpropylamino

(9) 3,3-diphenylpropylamino

(10) phenylamino

(11) 3-chlorophenylamino

(12) 4-methylphenylamino

(13) cyclopropylamino

(14) cyclopentylamino

(15) cyclohexylamino

(16) cycloheptylamino

(17) cyclooctylamino

(18) cyclododecylamino

(19) 2-methylcyclohexylamino

(20) 3-methylcyclohexylamino

(21) cis-4-methylcyclohexylamino

(22) trans-4-methylcyclohexylamino

(23) cis-4-tert-butylcyclohexylamino

(24) trans-4-tert-butylcyclohexylamino

(25) 4-hydroxycyclohexylamino

(26) 2-methoxycyclohexylamino

(27) 4-ethylcyclohexylamino

(28) 2,6-dimethylcyclohexylamino

(29) N-methylcyclohexylamino

(30) N,N-dicyclohexylamino

(31) endo-2-norbornylamino (or endo-bicyclo[2.2.1]-heptan-2-amino)

(32) exo-2-norbornylamino (or exo-bicyclo[2.2.1]heptan-2-amino)

(33) 1-adamantylamino

(34) 2-adamantylamino

(35) 1-noradamantylamino

(36) (1R)-bornylamino

(37) (1R)-isobornylamino

(38) spiro[5.5]undecanylamino

(39) cyclohexylmethylamino

(40) 1-adamantylmethylamino

(41) (2-tetrahydrofuranyl)methylamino

(42) 2-(N-methyl-2-pyrrolyl)ethylamino

(43) 2-(2-pyridinyl)ethylamino

(44) (2-indolyl)methylamino

(45) N-methyl(2-indolyl)methylamino

(46) 2-(3-indolyl)ethylamino

(47) N-methyl-2-(3-indolyl)ethylamino

(48) 4-(N-benzylpiperidinyl)amino

(49) 3-quinuclidylamino

(50) exo-bicyclo[3.2.1]octan-2-amino

(51) bicyclo[2.2.2]octan-2-amino

(52) 3-chlorobicyclo[3.2.1]oct-3-en-2-amino

(53) bicyclo[2.2.2]oct-2-en-5-amino

(54) exo-bicyclo[3.2.1]octan-3-amino

(55) endo-bicyclo[3.2.1]octan-3-amino

(56) endo-7-oxabicyclo[2.2.1]heptan-2-amino

(57) exo-7-oxabicyclo[2.2.1]heptan-2-amino

(58) endo-tricyclo[5.2.1.0.sup.2,6]decan-8-amino

(59) N-ethyl-1-adamantylamino

(60) tricyclo[2.2.1.0.sup.2,6]heptan-3-amino

(61) bicyclo[3.3.1]nonan-9-amino

(62) endo-1,3,3-trimethylbicyclo[2.2.1]heptan-2-amino (or fenchylamino)

(63) (1R, 2S-endo)-(+)-bicyclo[2.2.1]heptan-2-amino

(64) (1R,2R-exo)-(-)-bicyclo[2.2.1]heptan-2-amino

(65) (1S,2R-endo)-(-)-bicyclo[2.2.1]heptan-2-amino

(66) (1S,2S-exo)-(+)-bicyclo[2.2.1]heptan-2-amino

(67) 1-piperidinylamino

(68) 1-pyrrolidinylamino

(69) 1-hexahydroazepinylamino

(70) 4-morpholinylamino

(71) 4-thiomorpholinylamino

(72) N-methyl-exo-bicyclo[2.2.1]heptan-2-amino

(73) N-ethyl-exo-bicyclo[2.2.1]heptan-2-amino

(74) N-propyl-exo-bicyclo[2.2.1]heptan-2-amino

Of the products of formula (I) above, those of formula (Ia) below are advantageous; in particular, the compounds of formula (Ia'): ##STR3## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 are as defined above for (I), R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl and R.sub.2 is a non-aromatic C.sub.3 -C.sub.15 carbocyclic radical or a saturated 5- to 8-membered heterocyclic radical selected from 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, 4-morpholinyl and 4-thiomorpholinyl, and their salts, are particularly advantageous.

Of the products of formula (I), those of formulae (Ia), (Ib), (Ic), (Id), (Ie) and (If) below, in which at least one of the substituents w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 is other than hydrogen, R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl, R.sub.2 is as defined above, R.sub.3 is hydrogen or a (C.sub.1 -C.sub.3)-alkyl group, R.sub.4 is hydrogen or methyl and R.sub.5 is a cycloalkyl-(C.sub.1 -C.sub.3)-alkyl, the cycloalkyl being C.sub.3 -C.sub.6, or a phenyl-(C.sub.1 -C.sub.3)-alkyl which is unsubstituted or substituted on the aromatic ring by a methyl group or a fluorine or chlorine atom, and their salts, where appropriate, are particularly advantageous.

In these latter particularly advantageous products,

when R.sub.1 is a (C.sub.1 -C.sub.6)-alkyl, the methyl, ethyl, propyl and isopropyl groups are preferred;

when R.sub.3 is a (C.sub.1 -C.sub.3)-alkyl, the methyl group is preferred;

the preferred groups R.sub.2 are non-aromatic C.sub.3 -C.sub.15 carbocyclic radicals which are unsubstituted or substituted by a (C.sub.1 -C.sub.4)-alkyl, especially methyl, ethyl, propyl, isopropyl or t-butyl, or by two or three methyl groups, for example a methyl-, ethyl- or t-butyl-cyclohexyl radical or a dimethyl- or trimethylcyclohexyl radical, cycloalkyl-(C.sub.1 -C.sub.3)- alkyl radicals in which the cycloalkyl is C.sub.3 -C.sub.6 ; (C.sub.1 -C.sub.3)-alkyl radicals substituted by a 2- or 3-indolyl group; 2- and 3-indolyl radicals; and 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, 4-morpholinyl and 4-thiomorpholinyl radicals; and

the preferred groups R.sub.5 are cyclohexylmethyl, cyclohexylethyl,

benzyl, 4-methylbenzyl and phenethyl radicals.

Of the products of formula (I) above, those of formula (i): ##STR4## in which R.sub.4, X and R are as defined-above for (I), and their salts, are very advantageous, especially when R.sub.4 is hydrogen or a methyl group or when R.sub.4 is hydrogen or methyl and X is a direct bond.

The compounds of formula (i) in which R.sub.4 is hydrogen or methyl, X is a direct bond and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a methyl group and R.sub.2 is a non-aromatic C.sub.3 -C.sub.15 carbocyclic radical or a saturated 5- to 8-membered heterocyclic radical selected from 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, 4-morpholinyl and 4-thiomorpholinyl, and their salts, are particularly preferred.

Especially preferred is the compound of formula (i) in which R.sub.4 is methyl, X is a direct bond and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen and R.sub.2 is 1-piperidinyl, as well as its pharmaceutically acceptable salts and their solvates.

Other particularly preferred compounds of formula (i) are those in which R.sub.4 is hydrogen or methyl, X is --(CH.sub.2).sub.x N(R.sub.3)-- and R is --NR.sub.1 R.sub.2, x being zero or one, R.sub.1 being hydrogen, R.sub.3 being hydrogen or a methyl group and R.sub.2 being a phenyl which is unsubstituted or substituted by one or two halogen atoms, a (C.sub.1 -C.sub.5)-alkyl group or a (C.sub.1 -C.sub.5)-alkoxy group, or a non-aromatic C.sub.3 -C.sub.15 carbocyclic radical, and their salts.

Of the compounds of formula (I), those of formula (ii): ##STR5## in which X and R are as defined above for (I) and w.sub.4 is a methyl or methoxy group, especially those of formula (ii) in which w.sub.4 is a methyl or methoxy group, X is a direct bond and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a methyl group and R.sub.2 is a non-aromatic C.sub.3 -C.sub.15 carbocyclic radical, and their salts, are also advantageous.

An advantageous subclass comprises the compounds of formula (ii) in which w.sub.4 is a methyl or methoxy group, X is a group --(CH.sub.2).sub.x N(R.sub.3)-- in which x is zero or one and R.sub.3 is hydrogen or a methyl group, and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen and R.sub.2 is a phenyl which is unsubstituted or substituted by one or two halogen atoms, a (C.sub.1 -C.sub.5)-alkyl group or a (C.sub.1 -C.sub.5)-alkoxy group, or a non-aromatic C.sub.3 -C.sub.15 carbocyclic radical, or their salts.

Other valuable compounds according to the present invention are those of formula (I) in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 and X are as defined above for (I) and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl group and R.sub.2 is a 2- or 3-indolyl-(C.sub.1 -C.sub.3)-alkyl group or a 2- or 3-indolyl group, and their salts.

Of the latter, the products of formula (iii): ##STR6## in which X is as defined above for (I), R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl and R.sub.2 is a 2- or 3-indolyl-(C.sub.1 -C.sub.3)-alkyl group or a 2- or 3-indolyl group, and either w.sub.2 is hydrogen and w.sub.4 is a methyl or methcxy group or w.sub.2 and w.sub.4 are a chlorine atom, and their salts, are particularly valuable.

Of the products included in formula (I) above, those of formula (iv): ##STR7## in which X and R are as defined above for (I) and g.sub.4 is a bromine atom or a methyl or trifluoromethyl, and their salts, are also

valuable.

In preferred products of formula (iv), the two chlorine atoms are in the 2,3-, 2,4-, 2,5- or 3,4-positions, and in these preferred products of formula (iv), those in which X is a direct bond and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl and R.sub.2 is a non-aromatic carbocyclic radical containing from 3 to 15 carlDon atoms are particularly preferred.

The salts, where appropriate, of the compounds according to the present invention, especially of those of formulae (I), (Ia'), (i), (ii) and (iii) above and (Ia), (Ib), (Ic), (Id), (Ie) and (If) below, include both those with mineral or organic acids which permit a suitable separation or crystallization of the products, such as picric acid or oxalic acid, and those with acids which form pharmaceutically acceptable salts such as the hydrochloride, hydrobromide, sulfate, hydrogensulfate, dihydrogenphosphate, methanesulfonate, methylsulfate, oxalate, maleate, fumarate, naphthalene-2-sulfonate, glyconate, gluconate, citrate, isethionate and paratoluenesulfonate.

According to another of its features, the present invention relates to a method of preparing the compounds (I), which comprises treating a pyrazole-3-carboxylic acid derivative of the formula ##STR8## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 are as defined for (I), or one of its activated forms, namely one of its esters or acid chlorides, * either with an amine of the formula HNR.sub.1 R.sub.2, in which R.sub.1 and R.sub.2 are as defined for (I), to give the amides of the formula ##STR9## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4, R.sub.1 and R.sub.2 are as defined for (I), * or optionally with a primary amine R.sub.3 NH.sub.2, in which R.sub.3 is as defined for (I), to give the intermediate amides (V) of the formula ##STR10## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 and R.sub.3 are as defined for (I), to give, by reduction with a metal hydride, the intermediate amines of the formula ##STR11## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 and R.sub.3 are as defined for (I), which are converted to the amide or urea of the formula ##STR12## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.2, R.sub.3 and R.sub.4 are as defined for (I), by reaction with an acid chloride of the formula R.sub.2 COCl or, respectively, an isocyanate of the formula R.sub.2 --N.dbd.C.dbd.O, in which R.sub.2 is as defined for (I), * or with a diphenylphosphoryl azide derivative in a basic medium, followed by an acid treatment, to give the intermediate amine of the formula ##STR13## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 are as defined for (I), which is reacted with an acid chloride R.sub.2 COCl or an isocyanate R.sub.2 --N.dbd.C.dbd.O to give respectively the amides and ureas of the formulae ##STR14## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 are as defined for (I) and R.sub.3 is hydrogen, the same compounds in which R.sub.3 is other than hydrogen being prepared from the above primary amine (VII) converted to a secondary amine of the formula ##STR15## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 are as defined for (I) and R'.sub.3 is (C.sub.1 -C.sub.2)-alkyl, which are then reacted with an acid chloride R.sub.2 COCl or an isocyanate R.sub.2 --N.dbd.C.dbd.O to give the amides and ureas of formulae (Id) and (Ie) as defined above in which R.sub.3 is other than hydrogen, * or with an organomanganous reagent R.sub.5 MnX.sub.1, in which R.sub.5 is as defined for (I) and X.sub.1 is a halogen, to give the ketone derivatives of the formula ##STR16## the resulting compounds then being converted to

one of their salts, where appropriate.

In a preferential procedure, the pyrazoles of formula (I) can be synthesized from the corresponding esters by conversion of the ester group to an amide, urea or ketone via the acid and the acid chloride.

Said esters are synthesized by applying the method described in Berichte, 1887, 20, 2185.

The reaction scheme for the preparation of the compounds (I) via their methyl or ethyl esters (Alk.dbd.CH.sub.3 or C.sub.2 H.sub.5) is represented by SCHEME 1 below: ##STR17##

The first step a) consists in preparing an alkali metal salt of an acetophenone derivative of formula (IV), in which R.sub.4 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 are as defined above for (I), to which an equimolar amount of diethyl oxalate is then added (step b) to give the ketoester of formula (III).

In the case where R.sub.4 .dbd.H, the alkali metal will preferably be sodium and the salt of the ketoester (III) (Alk.dbd.CH.sub.3) will be obtained according to Bull. Soc. Chim. Fr., 1947, 14, 1098, using sodium methylate in methanol to perform step a).

In the case where R.sub.4 .dbd.CH.sub.3, the alkali metal will preferably be lithium and the salt of the ketoester (III) (Alk.dbd.C.sub.2 H.sub.5) will be obtained according to J. Heterocyclic Chem. 1989, 26, 1389, using the lithium salt of hexamethyldisilazane in ethyl ether to perform step a).

The alkali metal salts (III) prepared in this way are then refluxed in acetic acid with an excess of a hydrazine derivative (step c). Precipitation in iced water gives the 3-pyrazole esters (IIa).

These esters (IIa) are then converted to their acids (IIb) by reaction with an alkaline agent, for example potassium hydroxide, followed by acidification (step d).

In SCHEME 1 above, the esters of formula (IIa) in which w.sub.2 and w.sub.4 are a chlorine atom, w.sub.3, w.sub.5 and w.sub.6 are hydrogen, g.sub.4 is a chlorine atom, g.sub.2, g.sub.3, g.sub.5 and g.sub.6 are hydrogen and Alk is a (C.sub.1 -C.sub.5)-alkyl, and the corresponding acids (IIb), are novel key intermediates for the preparation of the particularly advantageous compounds (i) and therefore represent a further feature of the invention; these compounds have formula (II'a) or (II'b): ##STR18##

When X is a direct bond, the amides according the invention of formula (Ia): ##STR19## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.1, R.sub.2 and R.sub.4 are as defined for (I), are prepared from a functional derivative of the acids (IIb), preferably a chloride, by the usual methods so that said acids (IIb) can be substituted by an amine of the formula HNR.sub.1 R.sub.2, prepared by the usual methods, to give the compounds (Ia) according to the invention.

For example, when it is desired to prepare a compound of formula (Ia) in which g.sub.2, g.sub.3, g.sub.5, g.sub.6, w.sub.3, w.sub.5 and w.sub.6 are hydrogen, g.sub.4, w.sub.2 and w.sub.4 are a chlorine atom, R.sub.4 is methyl, R.sub.1 is hydrogen and R.sub.2 is 1-piperidinyl (namely N-piperidino-5-(4-chlorophenyl)-1(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide), a functional derivative of 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid (a compound of formula (II'b) in which R.sub.4 is methyl) is reacted with

1-aminopiperidine in an organic solvent in the presence of a base. The acid chloride, the anhydride, the mixed anhydride, a straight or branched C.sub.1 -C.sub.4 alkyl ester, an activated ester such as p-nitrophenyl ester, or the free acid appropriately activated, for example by N,N-dicyclohexylcarbodiimide or benzotriazol-N-oxotris(dimethylamino)phosphonium hexafluorophosphate (BOP) can be used as the functional derivative of the acid.

Thus, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl-4-methyl-pyrazole-3-carboxylic acid chloride, obtained by reaction of thionyle chloride with 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid, can be reacted with 1-aminopiperidine in a solvent such as dichloromethane in an inert atmosphere, at a temperature between 0.degree. C. and room temperature, in the presence of a base such as triethylamine.

Alternately, the mixed anhydride of 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid can be prepared by reaction of ethylchloroformate with the said acid in the presence of a base such as triethylamine, and then reacted with 1-aminopiperidine in a solvent such as dichloromethane in an inert atmosphere, at a temperature between 0.degree. C. and room temperature, in the presence of a base such as triethylamine.

When X is a group --(CH.sub.2).sub.x N(R.sub.3)--, in which x and R.sub.3 are as defined for (I), the amides and the ureas according to the invention of formulae (Ib) and (Ic): ##STR20## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.2, R.sub.3 and R.sub.4 are as defined for (I), are prepared from the above-described ester (IIa) according to SCHEME 2 below: ##STR21##

The conversion of the ester (IIa) to the intermediate amide (V) can be effected for example via the corresponding acid chloride, the latter being reacted with an amine R.sub.3 NH.sub.2 in an alkanol such as ethanol.

The reduction of the amide (V) to the amine (VI) is then effected by means of a metal hydride such as lithium aluminum hydride or, preferably, by means of the complex BH.sub.3 -THF in solution in THF under reflux. The amine (VI) is then converted to the amide (Ib) or the urea (Ic) according to the invention by the conventional methods, for example by reaction with an acid chloride R.sub.2 COCl or an isocyanate R.sub.2 --N.dbd.C.dbd.O, respectively.

The amides and the ureas according to the invention of formulae (Id) and (Ie): ##STR22## in which g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6, w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and R.sub.2, R.sub.3 and R.sub.4 are as defined for (I), are prepared from the previously obtained pyrazole-3-carboxylic acids according to SCHEME 3 below: ##STR23##

The acids (IIb) are converted to the corresponding amines (VII) by means of a Curtius reaction, for example using diphenylphosphoryl azide in a basic medium, followed by a treatment with a strong acid such as hydrochloric acid or trifluoroacetic acid, as described in Synthesis, 1990, 295. The amines (VII) are then converted to the amides (Id) or ureas (Ie) according to the invention by the usual methods, for example by reaction with an acid chloride R.sub.2 COCl in the case of (Id) where R.sub.3 .dbd.H, or with an isocyanate R.sub.2 --N.dbd.C.dbd.O in the case of (Ie) where R.sub.3 .dbd.H.

Alternatively, the ureas (Ie) where R.sub.3 .dbd.H can be prepared by the reverse reaction: the acids (IIb) are converted to corresponding

isocyanates (VIIc) as described in J. Org. Chem. 1961, 26, 3511, according to SCHEME 4 below.

Reaction of the isocyanates (VIIc) with an amine R.sub.2 NH.sub.2 then gives the ureas (Ie) directly. ##STR24##

To prepare the compounds (Id) and (Ie) in which R.sub.3 is other than hydrogen, the primary amines (VII) are first converted to secondary amines (VIIb) by a reaction sequence such as reaction with an acid chloride R'.sub.3 COCl (where R'.sub.3 .dbd.(C.sub.1 -C.sub.2) alkyl), followed by reduction of the amide (VIIa) obtained, for example by reaction with BH.sub.3 in THF. In the case where R.sub.3 is a methyl, it is preferable to react the amines (VII) with tert-butyl dicarbonate, (BOC).sub.2 O, or with a mixture of formic acid and acetic anhydride, giving respectively the carbamate (VIIa, Z.dbd.OtBu) or the formamide (VIIa, Z.dbd.H), which products are then reduced, for example with LiAlH.sub.4, to give the amines (VIIb, R.sub.3 .dbd.CH.sub.3).

The secondary amines (VIIb) are then converted to the amides (Id) or ureas (Ie) according to the invention as described above.

The ketone derivatives according to the invention of formula (If): ##STR25## in which g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6, w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and R.sub.4 and R.sub.5 are as defined for (I), are preferably prepared from the above-described pyrazole-3-carboxylic acids (IIb) according to SCHEME 5 below: ##STR26##

The acids (IIb) are converted to the acid chlorides by the conventional methods; the latter are then converted to the ketone derivatives (If) according to the invention by reaction with an appropriate organomanganous reagent R.sub.5 MnX.sub.1, in which R.sub.5 is as defined for (I) and X.sub.1 is a halogen, preferably a chlorine atom, for example using the method described in Tetrahedron Letters, 1989, 30, 7369.

Alternatively, the ketone derivatives (If) can be prepared from the acids (IIb) via the nitriles (IIc) according to SCHEME 6 below: ##STR27##

(IIb) is converted to (IIc) by a conventional method such as, for example, conversion to the acid chloride followed by amination (NH.sub.3/ THF/water) and dehydration of the amide obtained, for example by treatment with CH.sub.3 SO.sub.2 Cl in pyridine as described in J. Am. Chem. Soc., 1955, 77, 1701.

The nitriles (IIc) obtained in this way are then treated with organometallic reagents, preferably organomagnesium reagents of the formula R.sub.5 MgX.sub.1, to give the ketone derivatives (If) after acid treatment.

The compounds of formula (I) obtained in this way are isolated, in the form of the free base or, where appropriate, a salt or a solvate, by the conventional techniques.

When the compound of formula (I) is obtained in the form of the free base, a salt is formed by treatment with the chosen acid in an organic solvent. Treatment of the free base, for example dissolved in an alcohol such as isopropanol, an ether such as diethylether or in acetone, with a solution of the chosen acid in the same solvent gives the corresponding salt, which is isolated by the conventional techniques. The hydrochloride, hydrobromide, sulfate, hydrogensulfate, dihydrogenphosphate, methanesulfonate, oxalate, maleate, fumarate, naphthalene-2-sulfonate and paratoluenesulfonate, for example, are prepared in this way.

When the reaction is complete, the compounds of formula (I) can be isolated in the form of one of their salts, where appropriate, for example the hydrochloride or the oxalate; in this case, if necessary, the free base can be prepared by neutralizing said salt with a mineral or organic base such as sodium or ammonium hydroxide or triethylamine, or with an alkali metal carbonate or bicarbonate such as sodium or potassium carbonate or bicarbonate, and converted into another salt such as the methanesulfonate, fumarate or naphtalene-2-sulfonate.

The acid (II'b) in which R.sub.4 is methyl, namely 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxylic acid can for example be prepared as illustrated below in route 1 or route 2: ##STR28##

The first step is carried out according to J. Heterocyclic Chem., 1989, 26, 1389. ##STR29##

The first step is carried out according to the method described by E. S. Schweizer in J. Org. Chem., 1987, 52, 1324-1332. The second step is carried out according to the method described by R. E. Tirpak et al. in J. Org. Chem., 1982, 47, 5099-5102.

The amines of formula HNR.sub.1 R.sub.2 are either commercially available, or described in the literature, or prepared by known methods according to the PREPARATIONS described below.

Preferred examples of these amines are those mentioned below:

(1) bicyclo[3.2.1]octan-2-ylamine prepared according to H. Maskill et al., J. Chem. Soc. Perkin II, 1984, 119; ##STR30##

(2) bicyclo[2.2.2]octan-2-ylamine prepared according to R. Seka et al., Ber. 1942, 1379; ##STR31##

(3) endo- and exo-bicyclo[3.2.1]octan-3-ylamine prepared according to H. Maskill et al., J. Chem. Soc. Perkin Trans. II, 1984, 1369; ##STR32##

(4) endo- and exo-7-oxabicyclo[2.2.1]heptan-2-ylamine prepared according to W. L. Nelson et al., J. Heterocyclic Chem., 1972, 9, 561; ##STR33##

(5) endo-tricyclo[5.2.1.0.sup.2,6]decan-8-amine prepared according to G. Buchbauer et al., Arch. Pharm., 1990, 323, 367; ##STR34##

(6) endo-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ylamine prepared according to Ingersoll et al., J. Am. Chem. Soc., 1951, 73, 3360; ##STR35##

(7) 3-methylcyclohexylamine prepared according to Smith et al., J. Org. Chem., 1952, 17, 294; ##STR36##

(8) 2,6-dimethylcyclohexylamine prepared according to Cornubert et al., Bull. Soc. Chim. Fr., 945, 12, 367; ##STR37##

(9) 2-methoxycyclohexylamine prepared according to Noyce et al., J. Am. Chem. Soc., 1954, 76, 768; ##STR38##

(10) 4-ethylcyclohexylamine prepared according to A. Shirahata et al., Biochem. Pharmacol., 1991, 41, 205; ##STR39##

(11) bicyclo[2.2.21]oct-2-en-5-amine prepared according to H. L. Goering et al., J. Am. Chem. Soc., 1961, 83, 1391; ##STR40##

(12) N-ethyl-1-adamantylamine prepared according to V. L. Narayanan et al., J. Med. Chem., 72, 15, 443; ##STR41##

(13) tricyclo[2.2.1.0.sup.2, 6]heptan-3-ylamine prepared according to G. Muller et al., Chem. Ber., 65, 98, 1097; ##STR42##

(14) N-methyl-exo-bicyclo[2.2.1]heptan-2-ylamine prepared according to W. G. Kabalka et al., Synth. Commun., 1991, 20, 231; ##STR43##

(15) 2-azabicyclo[2.2.1]heptan-2-yl-amine prepared according to J. Am. Chem. Soc. 1982, 104, 5292, starting from 2-azabicyclo[2.2.1]heptane prepared according to Chem. Ber., 1983, 116, 1081. ##STR44##

(16) 2-azabicyclo [2.2.2]octan-2-yl-amine prepared according to J. Am. Chem. Soc. 1982, 104, 5292. ##STR45##

The amines R.sub.3 NH.sub.2 are commercially available or are prepared by known methods.

The acid chlorides R.sub.2 COCl are commercially available or are prepared from the corresponding acids by known methods.

The isocyanates R.sub.2 --N.dbd.C.dbd.O are also commercially available or are prepared from the corresponding amines (reaction with phosgene) or corresponding acids (Curtius rearrangement) by known methods.

The compounds according to the invention were subjected to biochemical tests.

The compounds (I) and their salts, where appropriate, exhibited a good affinity in vitro for the cannabinoid receptors in tests performed under the experimental conditions ,described by Devane et al., Molecular Pharmacology, 1988, 34, 605-613.

The compounds according to the invention also possess an affinity for the cannabinoid receptors present on preparations of electrically stimulated, isolated organs. These tests were performed on the guinea-pig ileum and on the mouse vas deferens according to Roselt et al., Acta Physiologica Scandinavia, 1975, 94, 142-144, and according to Nicolau et al., Arch. Int. Pharmacodyn., 1978, 236, 131-136.

In particular, the compound of formula (I) in which g.sub.2, g.sub.3, g.sub.5, g.sub.6, w.sub.3, w.sub.5 and w.sub.6 are hydrogen, w.sub.2 and w.sub.4 are a chlorine atom, R.sub.4 is methyl, X is a direct bond and R is 1-piperidinylamino (namely N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide), or one of its pharmaceutically acceptable salts, exhibits a very good affinity for the central cannabinoid receptors. This compound is a potent and selective antagonist of the central cannabinoid receptors and has a Ki of about 2 nM. It is from 500 to 1000 times more active on the central receptor as on the peripheral receptor; it is also active upon oral administration and penetrates the blood-brain barrier. The good penetration of this compound in the central nervous system as well as its antagonist character are confirmed by the results obtained with the model of the antagonism of hypothermia induced by an agonist of cannabinoid receptors. Especially, this compound antagonizes the hypothermia induced by WIN 55 212-2 in mice with an ED.sub.50 of 0.3 mg/kg i.p. and 0.4 mg/kg per os. In this test (Pertwee R. G., 1985:263-277; in Marijuana 84, Ed. Harvey, D. Y., IRL Press, Oxford), the above compound exerted its action for 8 to 10 hours after oral administration of a dose of 3 mg/kg.

In addition, the above compound, upon subcutaneous administration, improves the memory capacities of rats in the test of the central memory (A Perio et al. in Psychopharmacology, 1989, 97, 262-268).

The compounds according to the invention are generally administered in dosage units.

Said dosage units are preferably formulated in pharmaceutical compositions in which the active principle is mixed with a pharmaceutical excipient.

Thus, according to another of its features, the present invention relates to pharmaceutical compositions in which a compound of formula (I) or one of its pharmaceutically acceptable salts is present as the active principle.

The compounds of formula (I) above and their pharmaceutically acceptable salts can be used in daily doses of 0.01 to 100 mg per kilogram of body weight of the mammal to be treated, preferably in daily doses of 0.1 to 50 mg/kg. In humans, the dose can preferably vary from 0.5 to 4000 mg per day, more particularly from 2.0 to 1000 mg, depending on the age of the subject to be treated or the type of treatment: prophylactic or curative.

In the pharmaceutical compositions of the present invention for oral, sublingual, subcutaneous, intramuscular, intravenous, transdermal, local or rectal administration, the active principles can be administered to animals and humans in unit forms of administration, mixed with conventional pharmaceutical carriers. The appropriate unit forms of administration include forms for oral administration, such as tablets, gelatin capsules, powders, granules and solutions or suspensions to be taken orally, forms for sublingual and buccal administration, aerosols, implants, forms for subcutaneous, intramuscular, intravenous, intranasal or intraocular administration and forms for rectal administration.

In the pharmaceutical compositions of the present invention, the active principle is generally formulated as dosage units containing from 0.5 to 1000 mg, preferably from 1 to 500 mg, more preferably from 2 to 200 mg of said active principle per dosage unit for daily administrations.

When preparing a solid composition in the form of tablets, a wetting agent such as sodium laurylsulfate can be added to the active principle optionally micronized, which is then mixed with a pharmaceutical vehicle such as silica, gelatin, starch, lactose, magnesium stearate, talc, gum arabic or the like. The tablets can be coated with sucrose, with various polymers or other appropriate substances or else they can be treated so as to have a prolonged or delayed activity and so as to release a predetermined amount of active principle continuously.

A preparation in the form of gelatin capsules is obtained by mixing the active principle with a diluent such as a glycol or a glycerol ester and pouring the mixture obtained into soft or hard gelatin capsules.

A preparation in the form of a syrup or elixir can contain the active principle together with a sweetener, which is preferably calorie-free, methyl-paraben and propylparaben as an antiseptic, a flavoring and an appropriate color.

The water-dispersible powders or granules can contain the active principle mixed with dispersants or wetting agents, or suspending agents such as polyvinyl-pyrrolidone, and also with sweeteners or taste correctors.

Rectal administration is effected using suppositories prepared with binders which melt at the rectal temperature, for example cacao butter or polyethylene glycols.

Parenteral, intranasal or intraocular administration is effected using

aqueous suspensions, isotonic saline solutions or sterile and injectable solutions which contain pharmacologically compatible dispersants and/or wetting agents, for example propylene glycol, butylene glycol, or polyethylene glycol.

Thus a cosolvent, for example an alcohol such as ethanol or a glycol such as polyethylene glycol or propylene glycol, and a hydrophilic surfactant such as Tween.RTM. 80, can be used to prepare an aqueous solution injectable by intravenous route. The active principle can be solubilized by a triglyceride or a glycerol ester to prepare an oily solution injectable by intramuscular route.

Transdermal administration is effected using multilaminated patches or reservoirs into which the active principle is in the form of an alcoholic solution.

Administration by inhalation is effected using an aerosol containing for example sorbitan trioleate or oleic acid together with trichlorofluoromethane, dichlorotetrafluoroethane or any other biologically compatible propellant gas.

The active principle can also be formulated as microcapsules or microspheres, optionally with one or more carriers or additives.

Among the prolonged-release forms which are useful in the case of chronic treatments, implants can be used. These can be prepared in the form of an oily suspension or in the form of a suspension of microspheres in an isotonic medium.

The active principle can also be presented in the form of a complex with a cyclodextrin, for example .alpha.-, .beta.- or .gamma.-cyclodextrin, 2-hydroxypropyl-.beta.-cyclodextrin or methyl-.beta.-cyclodextrin.

The compounds of formula (I) formulated in this way can be used for the treatment of immunomodulation, migraine, asthma, epilepsy, glaucoma, Parkinson's disease, dyskinesia, neuropathy, memory and thymic disorders, vomiting, ischemia, angor, orthostatic hypotension, cardiac insufficiency, stress, anxio-depressive disorders or psychosomatic-induced disorders.

Especially, the compound of formula (Ia) in which g.sub.2, g.sub.3, g.sub.5, g.sub.6, w.sub.3, w.sub.5 and w.sub.6 are hydrogen, g.sub.4, w.sub.2 and w.sub.4 are a chlorine atom, R.sub.4 is methyl, R.sub.1 is hydrogen and R.sub.2 is 1-piperidinyl (namely N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide), as such or optionally in the form of a pharmaceutically acceptable salt or a solvate, can be used as the active principle of drugs intended for the treatment of the diseases of the central nervous system in mammals, thanks to its remarkable properties, especially its high affinity, its selectivity towards the central receptor as well as its capacity to penetrate the blood-brain barrier.

The toxicity of the above compound is compatible with its use as a psychotropic drug, especially for the treatment of thymic disorders, anxiety disorders, mood disorders, vomiting, memory disorders, cognitive disorders, neuropathies, migraine, stress, psychosomatic-induced diseases, epilepsy, dyskinesia or Parkinson's disease.

The above compound can also be used as a drug for the treatment of appetite disorders, especially as an anorexic, for the treatment of schizophrenia, delirious disorders, psychotic disorders in general as well as for the treatment of disorders associated with the use of psychotic substances. Furthermore, the above compound can be used in cancer chemotherapy.

The use of the above compound as a drug for the treatment of appetite disorders, anxiety disorders, mood disorders, schizophrenia, psychotic disorders, memory disorders, cognitive disorders and dyskinesia, as well as its use in cancer chemotherapy, constitute a further feature of the present invention.

DETD The following Examples illustrate the invention without however implying a limitation.

The melting or decomposition points of the products, m.p., were measured in a capillary tube with a Tottoli apparatus; in some cases, differential scanning calorimetry (DSC) was used to measure the melting temperature.

The following abbreviations are used in the preparations and in the examples:

THF: tetrahydrofuran

Et.sub.2 O or ether: diethyl ether

iPr.sub.2 O or iso ether: diisopropyl ether

EtOH: ethanol

AcOEt: ethyl acetate

MeOH: methanol

DCM: dichloromethane

KOH: potassium hydroxide

AcOH: acetic acid

HCl: hydrochloric acid

NaCl: sodium chloride

RT: room temperature

DSC: differential scanning calorimetry

M.p.: melting point

CH.sub.2 Cl.sub.2 : dichloromethane

Na.sub.2 CO.sub.3 : sodium carbonate

MgSO.sub.4 : magnesium sulfate

The following abbreviations are used in the interpretation of the NMR spectra:

s: singlet

d: doublet

t: triplet

q: quadruplet

m: unresolved signals or multiplet.

The enantiomeric excess of the optically active amines, e.e., was determined by .sup.19 F NMR after reaction with the chloride of S(+) Mosher's acid according to J. Org. Chem., 1969, 34, 2543.

The optical rotations, [.alpha.].sub.D.sup.20, were measured at c=1 in ethanol.

PREPARATIONS

A. AMINES NHR.sub.1 R.sub.2

1. (1R,2S-endo)-(+)-Bicyclo[2.2.1]heptan-2-yl-amine

(1R,2S-endo)-(-)-Bicyclo[2.2.1]heptane-2-carboxylic acid is prepared according to Tetrahedron Letters, 1985, 26, 3095.

By means of a Curtius reaction carried out according to J. Org. Chem., 1961, 26, 3511, this is then converted to the corresponding (1R, 2S-endo)-(+)-amine.

[.alpha.].sub.D.sup.20 32 +13.4.degree. (c=1, EtOH).

e.e.>95%, .delta.(CF.sub.3)=6.67 ppm relative to CF.sub.3 CO.sub.2 H.

2. (1R,2R-exo)-(-)-Bicyclo[2.2.1]heptan-2-yl-amine

The (1R,2S-endo)-(-)-bicyclo[2.2.1]heptane-2-carboxylic acid prepared in the previous Example is converted to its (1R,2R-exo)-(-) isomer according to J. Am. Chem. Soc., 1983, 105, 950, and then converted to the corresponding (1R,2R-exo)-(-)-amine as described in the previous Example.

[.alpha.].sub.D.sup.20 =-17.7.degree. (c=1, EtOH).

e.e.>94% (determined as above, .delta.(CF.sub.3)=6.81 ppm).

3. (1S,2R-endo)-(-)-Bicyclo[2.2.1]heptan-2-ylamine

(1S,2R-endo)-(+)-Bicyclo[2.2.1]heptane-2-carboxylic acid is prepared according to Tetrahedron Letters, 1989, 30, 5595, and then converted to the corresponding (1S,2R-endo)-(-)-amine as described above.

e.e.>95% (determined as above, .delta.(CF.sub.3)=6.62 ppm).

4. (1S,2S-exo)-(+)-Bicyclo[2.2.1]heptan-2-ylamine

The (1S,2R-endo)-(+)-acid prepared in the previous Example is converted to its (1S,2S-exo)-(+) isomer according to according to J. Am. Chem. Soc., 83, 105, 950, and this is then converted to the corresponding (1S,2S-exo)-(+)-amine as described above.

e.e.>94% (determined as above, .delta.(CF.sub.3)=6.91 ppm).

5. exo-3-Chlorobicyclo[3.2.1]oct-3-enyl-2-amine

0.4 g of PtO.sub.2 is added to a solution of 6.1 g of exo-3-chloro-2-azidobicyclo[3.2.1]oct-3-ene, obtained according to J. Chem. Soc. Perkin Trans. II, 1984, 119, in 600 ml of ethanol and 60 ml of CHCl.sub.3 and hydrogenation is carried out in a Parr apparatus at 4 bar and room temperature until the azide group has disappeared. After filtration on Celite, the reaction mixture is evaporated and the residue is crystallized from an ethanol/CHCl.sub.3 mixture to give 0.49 g of the

hydrochloride of the expected amine.

M.p.>240.degree. C.

6. N-Ethyl-exo-bicyclo[2.2.1]heptan-2-ylamine

6.1. N-Acetyl-exo-bicyclo[2.2.1]heptan-2-ylamine

A solution of 3.50 ml of acetyl chloride in 10 ml of CH.sub.2 Cl.sub.2 is added dropwise to a solution of 5.00 g of exo-bicyclo[2.2.1]heptan-2-ylamine and 6.90 ml of triethylamine in 50 ml of CH.sub.2 Cl.sub.2, cooled to 0.degree. C. After stirring for 16 hours at room temperature, the mixture is poured into 100 ml of iced water and the organic phase is separated off and washed with a 5% solution of HCl, then with water and then with a saturated solution of NaCl. After drying over MgSO.sub.4 and evaporation of the solvents, 5.80 g of the expected acetamide are obtained.

M.p.=128.degree. C.

6.2. N-Ethyl-exo-bicyclo[2.2.1]heptan-2-ylamine

A solution of 5.10 g of the above derivative in 30 ml of THF is added dropwise to a suspension of 2.18 g of LiAlH.sub.4 in 30 ml of THF, cooled to 0.degree. C., and the mixture is then refluxed for 8 hours. It is hydroyzed at 0.degree. C. with 2.2 ml of water, then 2.2 ml of a 15% solution of NaOH and then 7.5 ml of water. After stirring for 15 minutes, the precipitate is filtered off and washed with THF, the filtrate is evaporated and the residue is then taken up in 50 ml of ethyl ether. This ether solution is extracted with 5% HCl; the aqueous phase obtained is neutralized with 30% NaOH and then extracted with ethyl ether. After washing with a saturated solution of NaCl, drying over MgSO.sub.4 and evaporation, 3.82 g of a pale yellow liquid are obtained. Dissolution in ethyl ether and treatment with a soluItion of gaseous HCl in anhydrous ethyl ether gives a white precipitate, which is filtered off, washed with ethyl ether and dried under vacuum to give 4.16 g of the hydrochloride of the expected amine.

M.p.=145.degree. C. (decomposition).

7. N-(n-Propyl)-exo-bicyclo[2.2.1]heptan-2-ylamine

7.1. N-Propionyl-exo-bicyclo[2.2.1]heptan-2-ylamine

This amide is obtained in the same way as the N-acetyl analog described in Example 6 above, using propionyl chloride instead of acetyl chloride.

7.2. N-(n-Propyl)-exo-bicyclo[2.2.1]heptan-2-ylamine

This amine is obtained starting from the above amide, in the same way as the N-ethyl analog described in the previous Example. Salification with HCl/Et.sub.2 O in an Et.sub.2 O/iPr.sub.2 O mixture gives the hydrochloride of the expected amine.

M.p.=230.degree. C. (decomposition).

8. Bicyclo[3.3.1]nonan-9-ylamine

8.1. Bicyclo[3.3.1]nonan-9-one oxime

A solution of 1.83 g of hydroxylamine hydrochloride and 2.95 g of sodium acetate in 22 ml of water is added to a solution of 2.43 g of bicyclo[3.3.1]-nonan-9-one in 9 ml of methanol and the mixture is refluxed for 24 hours. After cooling, it is extracted with ethyl ether

and the organic phases are washed with a saturated solution of NaCl, then a 5% solution of Na.sub.2 CO.sub.3 and the water, dried over MgSO.sub.4 and evaporated to give 3.00 g of oxime.

M.p.=151.degree. C.

8.2. Bicyclo[3.3.1]nonan-9-ylamine

0.20 g of PtO.sub.2 is added to a solution of 1.00 g of oxime in 250 ml of ethanol and 4 ml of CHCl.sub.3 and hydrogenation is carried out in a Parr apparatus at 6 bar and room temperature for 18 hours. After filtration on Celite, the solvents are evaporated off and the residue is crystallized from an ethanol/heptane mixture to give 0.55 g of the hydrochloride of the expected amine.

M.p.>240.degree. C.

EXAMPLE 1

N-(2-Adamantyl)-1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide ##STR46##

A) Sodium salt of methyl 4-chlorobenzoylpyruvate

12 g of sodium are dissolved in 250 ml of anhydrous methanol. A mixture of 64.6 ml of 4-chloroacetophenone and 67.1 ml of diethyl oxalate in 600 ml of methanol is then added, the temperature being kept below 10.degree. C. The reaction mixture is then stirred at room temperature for 3 hours, after which 1 l of dry ether is added. Stirring is continued for 20 minutes, the mixture is filtered and the precipitate is washed with ether and dried under vacuum to give 74.6 g of the expected sodium salt.

B) Methyl 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylate

A suspension of 26.3 g of the sodium salt obtained above and 23.5 g of 2,4-dichlorophenylhydrazine hydrochloride in 250 ml of acetic acid is refluxed for 4 hours. After cooling, the mixture is poured on to 250 g of ice and the crystals obtained are filtered off, washed with water and dried under vacuum to give 26.3 g of ester.

M.p.=167.degree. C.

C) 1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid

A solution of 3.70 g of KOH in 35 ml of water is added to a solution of 10.0 g of the ester obtained above in 35 ml of methanol. The mixture is refluxed for 4 hours, cooled to room temperature, poured into 100 ml of water and then neutralized with a 5% solution of HCl. The crystals obtained are filtered off, washed with water and then with pentane and dried under vacuum to give 9.50 g of acid.

M.p.=185.degree. C.

D) 1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylic acid chloride

5.8 ml of thionyl chloride are added to a suspension of 9.50 g of the acid obtained above in 100 ml of toluene and the mixture is refluxed for 3 hours. The solvent is then evaporated off, the residue is subsequently taken up in 50 ml of toluene and the solvent is evaporated off again (procedure repeated twice) to give 8.28 g of acid chloride.

E) N-(2-Adamantyl)-1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide

A solution of 0.50 g of the acid chloride obtained above in 10 ml of CH.sub.2 Cl.sub.2 is added dropwise to a solution of 01.30 g of adamantan-2-amine hydrochloride and 0.41 ml of triethylamine in 10 ml of CH.sub.2 Cl.sub.2, cooled to 0.degree. C. The mixture is subsequently stirred at room temperature for 16 hours and then poured into 30 ml of iced water. The mixture is extracted with CH.sub.2 Cl.sub.2 and the organic phase is washed successively with a 5% solution of HCl, water, a 5% solution of Na.sub.2 CO.sub.3 and then a saturated solution of NaCl. After drying over MgSO.sub.4 and evaporation of the solvent, the crude product is crystallized from hot benzene to give 0.32 g of white crystals.

M.p.=203.degree. C.

EXAMPLE 2

N-(trans-4-Hydroxycyclohexyl)-1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide ##STR47##

A) trans-4-Trimethylsilyloxycyclohexylamine

A solution of 1.85 ml of chlorotrimethylsilane in 10 ml of CH.sub.2 Cl.sub.2 is added dropwise to a solution of 2.0 g of trans-4-hydroxycyclohexylamine hydrochloride and 4.05 ml of triethylamine in 20 ml of CH.sub.2 Cl.sub.2, cooled to 0.degree. C. After stirring for 16 hours at room temperature, the mixture is hydrolyzed with water and extracted. The organic phase is washed successively with water, a 5% solution of Na.sub.2 CO.sub.3 and saturated NaCl. After drying over MgSO.sub.4 and evaporation of the solvents, 1.43 g of amine (colorless liquid) are obtained.

B) N-(trans-4-Hydroxycyclohexyl)-1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide

A solution of 0.60 g of the acid chloride prepared above according to Example 1D) in 10 ml of CH.sub.2 Cl.sub.2 is added dropwise to a solution of 0.35 g of trans-4-trimethylsilyloxycyclohexylamine and 0.32 ml of triethylamine in 10 ml of CH.sub.2 Cl.sub.2, cooled to 0.degree. C. After stirring for 16 hours at room temperature, the mixture is poured into 30 ml of iced water and extracted with CH.sub.2 Cl.sub.2. The organic phase is washed successively with 5% HCl and a saturated solution of NaCl and then dried over MgSO.sub.4 and evaporated. The crude product is dissolved in 15 ml of THF; 15 ml of 5% HCl are added to the solution and the mixture is stirred for 1 hour. It is then extracted with ether and the extract is washed with water and then dried over MgSO.sub.4, evaporated and crystallized from CH.sub.3 OH to give 0.20 g of the expected pyrazole.

M.p.=209.degree. C.

The compounds described in TABLES I to XII below are prepared by the procedure of EXAMPLE 1 above, starting for example from the acid or ester derivatives described below in TABLE A.

TABLE A

##STR48##

m.p.; .degree.C.

m.p.; .degree.C.

w.sub.2

w.sub.3	w.sub.4	w.sub.5	w.sub.6	g.sub.2	g.sub.4	Z = H	Z = CH.sub.3
H	H	CH.sub.3					
			H	H	H	Cl	185	98
H	Cl	Cl	H	H	H	Cl	162	147
H	Cl	Cl	H	H	H	CH.sub.3		
							188	145
Cl	H	H	Cl	H	H	CH.sub.3		
							232	132
Cl	H	H	Cl	H	H	CF.sub.3		
							214	179
Cl	Cl	H	H	H	H	CH.sub.3		
							214	101
H	H	CH.sub.3						
			H	H	Cl	Cl	188	102
H	H	Cl	H	H	Cl	Cl	224	118
H	H	OCH.sub.3						
			H	H	H	Cl	168	--
Cl	H	Cl	H	Cl	H	Cl	255	214
Cl	H	Cl	H	H	H			
					##STR49##			
							115	138
Cl	H	Cl	H	H	H	Br	188	177
H	H	NO.sub.2						
			H	H	H	CH.sub.3		
							106	166

TABLE I

##STR50##	(Ia)	
##STR51##		
##STR52##	##STR53##	
3	NH(CH.sub.2).sub.2	CH.sub.3
		100
4		
##STR54##		102
5		
##STR55##		60
6	NH(CH.sub.2).sub.4	CH.sub.3
		97
7		
##STR56##		152
8		
##STR57##		(1)
9		
##STR58##		152
10		
##STR59##		148
11		
##STR60##		162
12		
##STR61##		83
13		
##STR62##		132
14		
##STR63##		186
##STR64##		165

```
16
      ##STR65##          134
17
      ##STR66##          144
18
      ##STR67##          174
19
      ##STR68##          188
20
      ##STR69##          120
21
      ##STR70##          208
22
      ##STR71##           81
23
      ##STR72##          122
24
      ##STR73##          188
25
      ##STR74##          194
26
      ##STR75##          190
27
      ##STR76##          183 +14,1.degree.
28
      ##STR77##          182 -14,1.degree.
29
      ##STR78##          178
30
      ##STR79##          191
31
      ##STR80##          185 +10,2.degree.
32
      ##STR81##          184 -10,6.degree.
33
      ##STR82##          170
34
      ##STR83##          198
35
      ##STR84##          182
36
      ##STR85##          188
37
      ##STR86##          141
38
      ##STR87##          197
39
      ##STR88##          209
40
      ##STR89##          164
41
      ##STR90##          184
42
      ##STR91##          180
43
      ##STR92##          233
44
      ##STR93##          220
45
      ##STR94##          156 +11,7.degree.
46
      ##STR95##          151 -61,6.degree.
47
      ##STR96##          168
```

48		
	##STR97##	108
49		
	##STR98##	161
50		
	##STR99##	154
51		
	##STR100##	112
52		
	##STR101##	159
53		
	##STR102##	149
54		
	##STR103##	125
55		
	##STR104##	220
57		
	##STR105##	158
58		
	##STR106##	234 HCl
59		
	##STR107##	96
60		
	##STR108##	95
61		
	##STR109##	179
62		
	##STR110##	172
63		
	##STR111##	215 (dec) HCl
64		
	##STR112##	184
65		
	##STR113##	195 (dec) HCl
66		
	##STR114##	158
67		
	##STR115##	147
68		
	##STR116##	186
69		
	##STR117##	205 HCl
70		
	##STR118##	136
71		
	##STR119##	208
72		
	##STR120##	162
73		
	##STR121##	139

(1) NMR spectrum of the compound of Example 8 (200 MHz, DMSO d.sup.6): 0.74 (3H, t, J = 5 Hz, CH.sub.3); 0.91 (3H, t, J = 5 Hz, CH.sub.3); 1.41-1.69 (12H, m, 6CH.sub.2); 3.43 (2H, t, NCH.sub.2); 3.66 (2H, s, NCH.sub.2); 7.06 (1H, s, H pyrazole); 7.29 (2H, d, J = 8 Hz, H ar); 7.49 (2H, d, J = 8 Hz, H ar); 7.62-7.77 (2H, m, H ar); 7.92 (1H, d, J = 2 Hz, ar).

TABLE II

##STR122## (Ia)

##STR123##

##STR124##

##STR125##

74	NH(CH.sub.2).sub.2 CH.sub.3	95
75	##STR126##	114
76	##STR127##	59
77	##STR128##	175
78	##STR129##	178
79	##STR130##	175
80	##STR131##	147

TABLE III

##STR132## ##STR133##	##STR134##	(Ia)	##STR135##
81	##STR136##	144	
82	##STR137##	165	
83	##STR138##	143	
84	##STR139##	155	
85	##STR140##	153	
86	##STR141##	129	
87	##STR142##	140	
88	##STR143##	148	
89	##STR144##	137	
90	##STR145##	63	
91	##STR146##	156	
92	##STR147##	149	-15,1.degree.
93	##STR148##	149	+15,1.degree.
94	##STR149##	(2)	
95	##STR150##	48	
96	##STR151##	57	
97	##STR152##	157	
98	##STR153##	168	
99	##STR154##	156	
100	##STR155##	112	

(2) NMR spectrum of the compound of Example 94 (200 MHz, DMSO d.sup.6): 1.14-1.80 (10H, m, norbornyl); 2.34 (3H, s, CH.sub.3 tolyl); 3.12 (3H, sb NCH.sub.3); 4.40 (1H, t, NCH norbornyl); 6.90 (1H, s, H pyrazole); 7.23-7.31 (2H, m, H ar); 7.71-7.77 (5H, m, H ar).

TABLE IV

##STR156##	(Ia) ##STR157## ##STR158##	##STR159##
101	##STR160##	154
102	##STR161##	149
103	##STR162##	136
104	##STR163##	165
105	##STR164##	134

TABLE V

##STR165##	(Ia) ##STR166## ##STR167##	##STR168##
106	##STR169##	205
107	##STR170##	175
108	##STR171##	214
109	##STR172##	240
110	##STR173##	124
111	##STR174##	124

TABLE VI

##STR175##	(Ia) ##STR176## ##STR177##	##STR178##
112	##STR179##	215
113	##STR180##	55
114	##STR181##	168

TABLE VII

##STR182##	(Ia)

##STR183##

##STR184##

##STR185##

115		
	##STR186##	193
116		
	##STR187##	168
117		
	##STR188##	152
118		
	##STR189##	216
119		
	##STR190##	154
120		
	##STR191##	102

TABLE VIII

##STR192## (Ia)

##STR193##

##STR194##

##STR195##

121		
	##STR196##	146
122		
	##STR197##	115
123		
	##STR198##	119
124		
	##STR199##	115
125		
	##STR200##	112

TABLE IX

##STR201## (Ia)

##STR202##

##STR203##

##STR204##

126		
	##STR205##	150
127		
	##STR206##	142
128		
	##STR207##	159
129		
	##STR208##	108

TABLE X

##STR209## (Ia)

##STR210##

##STR211##

##STR212##

130	NH(CH.sub.2).sub.2	CH.sub.3
		144
131		

	##STR213##	115
132		
	##STR214##	123
133		
	##STR215##	108
134		
	##STR216##	120
135		
	##STR217##	169
136		
	##STR218##	68
137		
	##STR219##	58
138		
	##STR220##	182
139		
	##STR221##	152

TABLE XI

##STR222## ##STR223##	##STR224##	##STR225##
140		
	##STR226##	260
141		
	##STR227##	191
142		
	##STR228##	182

TABLE XII

##STR229## ##STR230##	##STR231##		(Ia) ##STR232##	##STR233## ##STR234##
143				
	##STR235##	Br	H	130
144				
	##STR236##	Cl	Cl	224
145				
	##STR237##	Br	H	148
146				
	##STR238##	Cl	Cl	245
147				
	##STR239##	Br	H	206
148				
	##STR240##	Cl	Cl	231
149				
	##STR241##	Br	H	201
150				
	##STR242##		##STR243## H	165
151				
	##STR244##	Br	H	209
152				

##STR245##

##STR246##

H 204

EXAMPLE 153

N-(2-Adamantyl)-1-(2,4-dichlorophenyl)-4-methyl-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide ##STR247##

A) Lithium salt of ethyl 2,4-dioxo-(4-chlorophenyl)butanoate

60 ml of a 1.0M solution of the lithium salt of hexamethyldisilazane in THF are introduced into 240 ml of anhydrous ether. The mixture is cooled to -78.degree. C. and a solution of 10.12 g of 4-chloropropiophenone in 50 ml of ether is introduced dropwise. After stirring for 30 minutes at -78.degree. C., a solution of 9.16 ml of diethyl oxalate in 50 ml of ether is introduced rapidly, the temperature is then allowed to rise and the mixture is stirred for 5 hours at room temperature. The pale yellow precipitate formed is filtered off, washed with ether and dried under vacuum to give 6.32 g of the expected salt.

B) Ethyl 1-(2,4-dichlorophenyl)-4-methyl-5-(4-chlorophenyl)-1H-pyrazole-3-carboxylate

This ester is obtained in the same way as in Example 1B) from the lithium salt obtained above, and is purified by recrystallization from isopropyl ether.

M.p.=105.degree. C.

C) Compound 153

This amide is obtained from the above ester in the same way as in Example 1C), 1D) and 1E) by conversion of the ester to the acid chloride, reaction of the latter with adamantan-2-amine and purification by recrystallizaticn from isopropyl ether.

M.p.=190.degree. C.

The amides described in TABLE XIII below are prepared by the procedure of Example 153 above.

TABLE XIII

##STR248## Example n.degree.	(Ia) NHR.sub.2	m.p.; .degree.C.
154	##STR249##	78
155	##STR250##	85
156	##STR251##	148
157	##STR252##	155
158	##STR253##	201

EXAMPLE 159

N-[1-(para-Tolyl)-5-(4-chlorophenyl)-1H-pyrazol-3-ylmethyl]-N-

methylcyclohexylcarboxamide ##STR254##

A) N-Methyl-1-(p-tolyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide

A solution of 0.50 g of 1-(4-methylphenyl)-5-(4-chlorophenyl)pyrazole-3-carboxylic acid chloride in ml of CH.sub.2 Cl.sub.2 is added dropwise to 100 ml of a 33% solution of methylamine in ethanol. After stirring for hours at room temperature, the mixture is concentrated under vacuum, the residue is taken up with a mixture of 5% Na.sub.2 CO.sub.3 +AcOEt, the organic phase is decanted, washed with a saturated solution of NaCl and dried over MgSO.sub.4 and the solvents are evaporated off. The residue is taken up in isopropyl ether and the crystals obtained are filtered off and dried under vacuum to give 0.44 g of the expected amide.

M.p.=138.degree. C.

B) N-Methyl-[1-(p-tolyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]methylamine

A solution of 8.76 g of the amide obtained above in 25 ml of anhydrous THF is added dropwise, at a temperature between 0.degree. and 5.degree. C., to 75 ml of a 1.0M solution of BH.sub.3 in THF. After the reaction mixture has returned to room temperature, it is refluxed for 16 hours and 18 ml of 6 N HCl are then run in, while cooling with an ice bath. The mixture is stirred for 1 and a half hours at room temperature, the THF is then distilled and the residue is concentrated under vacuum. The reaction mixture is then rendered alkaline to pH 9-10 with NaOH pellets; extraction is carried out with ethyl acetate, the extract is dried over MgSO.sub.4, the solvents are evaporated off and the crude product obtained is purified by chromatography on silica gel (300 g) using CH.sub.2 Cl.sub.2 /CH.sub.3 OH 97/3 (v/v) as the eluent to give 6.0 g of amine.

M.p.=85.degree. C.

C) Compound 159

0.62 ml of triethylamine and then a solution of 0.23 g of cyclohexanoic acid chloride in 5 ml of CH.sub.2 Cl.sub.2 are added successively to a solution of 0.46 g of the above amine in 10 ml of CH.sub.2 Cl.sub.2. After stirring for 15 minutes at room temperature, the reaction mixture is concentrated under vacuum and the residue is taken up in 30 ml of water and extracted with ethyl acetate. The organic phase is washed successively with 5% Na.sub.2 CO.sub.3, water and then a saturated solution of NaCl and dried over MgSO.sub.4 and the solvents are then evaporated off. The crude product is purified by chromatography on silica gel (25 g) using toluene/AcOEt 70/30 (v/v) as the eluent. The pure product fractions are concentrated under vacuum and the residue is recrystallized from isopropyl ether to give 0.38 g of amide.

M.p.=124.degree. C.

The amides described in TABLES XIV and XV below are prepared by the procedure of EXAMPLE 159 above.

TABLE XIV

##STR255##	(Ib)		
##STR256##			
##STR257##			
		##STR258##	
160			
##STR259##	178		
161			

	##STR260##	148
162		
	##STR261##	148
163		
	##STR262##	123
164		
	##STR263##	142
165		
	##STR264##	175
166		
	##STR265##	225
167		
	##STR266##	155
168		
	##STR267##	228

TABLE XV

##STR268##		(Ib)
##STR269##		
	##STR270##	
		##STR271##
169		
	##STR272##	103
170		
	##STR273##	166
171		
	##STR274##	165

EXAMPLE 172

N-[1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-ylmethyl]-N'-(4-chlorophenyl)urea ##STR275##

A) 1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide

This amide is obtained in the same way as in Example 159A) by reacting the acid chloride described in Example 1D) with a saturated solution of ammonia in ethanol.

M.p.=178.degree. C.

B) [1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]methylamine

This amine is obtained in the same way as in Example 159B) by reducing the amide obtained above with BH.sub.3 in THF.

C) Compound 172

0.20 g of 4-chlorophenyl isocyanate is added to a solution of 0.45 g of the above amine in 10 ml of toluene and the reaction mixture is stirred at room temperature for 16 hours. The solvent is evaporated off, the residue is taken up in 20 ml of ethyl acetate, washed with water and then dried over MgSO.sub.4 and the solvents are evaporated off. The residue is purified by chromatography on silica gel (20 g) using toluene/AcOEt 60/40 (v/v) as the eluent. Concentration of the pure product fractions gives a residue, which is recrystallized from an isopropanol/isopropyl ether mixture to give 0.18 g of the expected urea.

M.p.=172.degree. C.

The ureas described in TABLE XVI below are prepared by the procedure of EXAMPLE 172 above.

TABLE XVI

##STR276## ##STR277## ##STR278##	(Ic) ##STR279## ##STR280## ##STR281##			
173				
##STR282##	Cl	Cl	122	
174				
##STR283##	Cl	Cl	88	
175				
##STR284##	Cl	Cl	120	
176				
##STR285##	Cl	Cl	157	
177				
##STR286##	Cl	Cl	157	
178				
##STR287##	Cl	Cl	138	
179				
##STR288##	H	CH.sub.3	183	
180				
##STR289##	H	CH.sub.3	148	

EXAMPLE 181

N-[1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]cyclohexylcarboxamide ##STR290##

A) N-(tert-Butoxycarbonyl)-[1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]amine

3.25 g of the 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)pyrazole-3-carboxylic acid obtained according to Example 1C) and then 1.32 ml of triethylamine are added to a solution of 2.05 ml of diphenylphosphoryl azide in 40 ml of anhydrous t-butanol and the reaction mixture is refluxed under nitrogen for 12 hours. After cooling, it is treated with a saturated solution of NaHCO.sub.3 and extracted with ethyl acetate. After washing with water and then with a saturated solution of NaCl, drying over MgSO.sub.4 and evaporation of the solvents, the crude product is purified by chromatography on 70-230 mesh silica gel using CH.sub.3 OH/CH.sub.2 Cl.sub.2 1/99 (v/v) as the eluent to give 1.09 g of the expected product.

B) 1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-ylammonium hydrochloride

1.09 g of the above product are dissolved in 20 ml of a saturated solution of HCl in EtOH, diluted to 50%, and the reaction mixture is refluxed for 2 hours. The solvent is then evaporated off and the residue is triturated in ethyl acetate under reflux and then filtered off and dried under vacuum to give 0.55 g of the hydrochloride.

C) Compound 181

A solution of 0.11 ml of cyclohexanecarboxylic acid chloride in 2 ml of CH.sub.2 Cl.sub.2 is added dropwise to a solution of 0.20 g of the hydrochloride obtained in the previous Example and 0.19 ml of triethylamine in 5 ml of CH.sub.2 Cl.sub.2. After stirring for 24 hours at room temperature, the mixture is washed successively with a 5% solution of HCl, water, a 5% solution of Na.sub.2 CO.sub.3 and then a saturated solution of NaCl and dried over MgSO.sub.4 and the solvents are then evaporated off. The crude product is crystallized from iPr.sub.2 O to give 0.12 g of the expected amide.

M.p.=213.degree. C.

EXAMPLE 182

N-Methyl-N-[1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]adamantyl-1-carboxamide ##STR291##

A) N-[1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]formamide

0.50 g of 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-ylamine, obtained in the previous Example, is added in small portions to a mixture of 4 ml of formic acid and 0.5 ml of acetic anhydride, cooled in an ice bath. After stirring for 30 min, the solvents are evaporated off under vacuum and the residue is taken up in isopropyl ether. The white solid obtained is filtered off, washed with isopropyl ether and dried under vacuum to give 0.49 g of the expected formamide.

M.p.=181.degree. C.

B) N-Methyl-[1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]amine

A solution of 1.15 g of the formamide obtained in the previous Example in 10 ml of anhydrous THF is added dropwise, at room temperature, to a suspension of 0.24 g of LiAlH.sub.4 in 40 ml of anhydrous THF. The mixture is then refluxed for 20 minutes, cooled to 0.degree. C. and hydrolyzed with 0.24 ml of water, then 0.24 ml of 15% NaOH and then 0.72 ml of water. After stirring for 20 minutes at room temperature, the mixture is filtered, the material on the filter is washed with THF and the filtrate is evaporated to dryness. The residue is taken up in isopropyl ether, filtered off and dried under vacuum to give 1.02 g of the expected amine.

M.p.=157.degree. C.

C) Compound 182

By following the procedure of Example 181C), reaction of the amine obtained above with adamantane-1-carboxylic acid chloride gives the expected amide, which is purified by chromatography on a silica column using AcOEt/toluene 7:93 as the eluent.

M.p.=65.degree. C.

TABLE XVII

##STR292##		(Id)	
Example n.degree.	R.sub.3	R.sub.2	m.p.; .degree.C.
183	H	##STR293##	284
184	H		

		##STR294##	291
185	H		
		##STR295##	164
186	CH.sub.3		
		##STR296##	127

EXAMPLE 187

N-Methyl-[1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]-N'-(4-chlorophenyl)urea ##STR297##

225 mg of 4-chlorophenyl isocyanate are added to a suspension of 0.40 g of 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-ylamine, obtained by neutralizing the hydrochloride obtained in Example 181B), in 15 ml of toluene and the mixture is heated at 40.degree. C. for 1 hour and then left to react at room temperature for 16 hours. The precipitate obtained is filtered off, washed with toluene and dried under vacuum to give 0.46 g of the expected urea. M.p.=215.degree. C.

EXAMPLE 188

N-[1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]-N'-(1-adamantyl)urea ##STR298##

A) A solution of 2.54 g of sodium azide in 10 ml of water is added to a solution of 10.0 g of the acid chloride obtained according to Example 1D) in 320 ml of acetone, cooled to 0.degree. C. After stirring for 1 hour at 0.degree. C., the precipitate obtained is filtered off, washed with acetone and then dried under vacuum to give 9.86 g of the expected acyl azide.

B) N-[1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]-N'-(1-adamantyl)urea

A solution of 1.00 g of the acyl azide obtained in the previous Example in 5 ml of toluene is refluxed for 30 minutes. After it has returned to room temperature, the resulting solution of isocyanate is treated with 0.39 g of adamantan-1-amine and the mixture is stirred for 1 and a half hours. The precipitate obtained is filtered off, washed with toluene and then isopropyl ether and subsequently purified by trituration in an acetone/methanol mixture. After drying under vacuum, 0.48 g of the expected urea is obtained.

M.p.=244.degree. C.

TABLE XVIII

##STR299##			(Ie)
Example n.degree.	R.sub.3	R.sub.2	m.p.; .degree.C.
189	H		
		##STR300##	227
190	CH.sub.3		
		##STR301##	144

EXAMPLE 191

1-Cyclolhexylmethyl [1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]ketone ##STR302##

2.5 ml of a 0.625M solution of MnLi.sub.2 Cl.sub.4 in THF (Tetrahedron,

1989, 45, 4163) are cooled to 0.degree. C., 3.12 ml of a 0.50M solution of methylcyclohexylmagnesium bromide in THF are added dropwise and the reaction mixture is then stirred at 0.degree. C. for 2 hours. It is then cooled to -10.degree. C. and a solution of 0.50 g of the acid chloride prepared according to Example 1D) in 8 ml of THF is added dropwise. The mixture is stirred at room temperature for 5 hours and then hydrolyzed with a saturated solution of NH.sub.4 Cl and extracted with ether and the extract is washed with water and then with a saturated solution of NaCl. After drying over MgSO.sub.4 and evaporation of the solvents, the crude product is purified by chromatography on 230-400 mesh silica gel using AcOEt/hexane 5/95 (v/v) as the eluent to give 0.09 g of the expected ketone.

M.p.=118.degree. C.

EXAMPLE 192

1-[1-(2,4-Dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazol-3-yl]-2-(4-methylphenyl)ethan-1-one ##STR303##

A) 1-(2,4-Dichlorophenyl)-3-cyano-5-(4-chlorophenyl)-pyrazole

A solution of 0.70 g of 1-(2,4-dichlorophenyl)-5-(4-chlorophenyl)-1H-pyrazole-3-carboxamide, obtained according to Example 172A), and 0.74 ml of mesyl chloride in 6 ml of pyridine is heated at 50.degree. C. for 8 hours. The solvent is evaporated off under vacuum and the residue is dissolved in 20 ml of CH.sub.2 Cl.sub.2. The resulting solution is washed successively with a 5% solution of HCl, then water and then a saturated solution of NaCl and dried over MgSO.sub.4 and the solvent is then evaporated off. The residue is crystallized from isopropyl ether to give 0.66 g of the expected nitrile.

M.p.=123.degree. C.

B) Compound 292

6.3 ml of a 1.0M solution of 4-methylbenzylmagnesium chloride in ethyl ether are added dropwise to a solution of 0.73 g of the above nitrile in 20 ml of ethyl ether. After a reaction time of 2 hours at room temperature, the mixture is hydrolyzed with 50 ml of 5% hydrochloric acid and the resulting two-phase mixture is stirred for 30 minutes. The pink precipitate formed is filtered off, washed with water and ethyl ether and then dissolved in 100 ml of CH.sub.2 Cl.sub.2 and the solution is stirred for 30 minutes in the presence of about 10 g of moist silica. The silica is then filtered off, the liltrate is evaporated and the residue is crystallized from a CH.sub.2 Cl.sub.2 /iPr.sub.2 O mixture to give 0.37 g of the expected ketone.

M.p.=175.degree. C.

TABLE XIX

Example n.degree.	R.sub.5	(If) m.p.; .degree.C.
193	##STR305##	129
194	##STR306##	152

EXAMPLE 195

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide

A) Lithium salt of ethyl 4-(4-chlorophenyl)-3-methyl-4-oxydo-2-oxobuten-3-oate

125 ml of a 1M solution of the lithium salt of hexamethyldisilazane in THF are added under a nitrogen atmosphere to 500 ml of ether. The mixture is cooled to -78.degree. C. and a solution of 21 g of 4-chloropropiophenone in 100 ml of ether is added dropwise. After stirring for 45 minutes, 19.2 ml of ethyl oxalate are added rapidly and the mixture is stirred for 16 hours while allowing the temperature to rise to room temperature. The precipitate formed is filtered off, washed with ether and dried under vacuum to give 12.6 g of the expected product.

B) Ethyl 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylate

9.8 g of 2,4-dichlorophenylhydrazine are added to a solution of 12.6 g of the lithium salt obtained above in 70 ml of ethanol and the mixture is stirred for 16 hours at room temperature. The precipate formed is filtered off, washed with ethanol and then ether and dried under vacuum to give 12.6 g of hydrazone. This is dissolved in 100 ml of acetic acid, the mixture is refluxed for 24 hours and then poured into 500 ml of iced water. The mixture is extracted with ethyl acetate, washed with water and then a saturated solution of NaCl. After drying over magnesium sulfate and evaporation under vacuum, the crude product is crystallized from isopropyl ether to give 9.6 g of the expected product. m.p.=124.degree. C.

C) 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid

A solution of 3.3 g of KOH in 70 ml of water is added to a solution of 9.6 g of the ester obtained above in 70 ml of methanol. The mixture is refluxed for 3 hours, poured into 200 ml of iced water and the reaction mixture is acidified to pH=1 upon addition of a 10% solution of HCl. The precipitate formed is filtered off, washed with water and dried under vacuum to give 0 8.8 g of the expected acid. m.p.=211.degree. C.

D) 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid chloride

5 ml of thionyl chloride are added to a suspension of 8.8 g of the acid obtained above in 90 ml of toluene, the mixture is refluxed for 3 hours and then evaporated to dryness under vaccum. The residue is taken up in 90 ml of toluene and the solvent is evaporated off again to give 8.0 g of the expected acid chloride which is used as such in the following step.

E) N-piperidino-5-(4-chlorophenyl)-1(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide

A solution of 8.0 g of the acid chloride obtained above in 80 ml of dichloromethane is added dropwise to a solution of 2.8 ml of 1-aminopiperidine and 3.6 ml of triethylamine in 100 ml of dichloromethane, cooled to 0.degree. C. The reaction mixture is stirred for 3 hours while allowing the temperature to rise to room temperature and then poured into 200 ml of iced water. The mixture is extracted with dichloromethane, washed with water and then a saturated solution of NaCl, dried over MgSO.sub.4 and evaporated under vaccum. The residue is purified by chromatography on silica gel using AcOEt/toluene (10/90; v/v) as the eluent. Crystallisation in isopropyl ether gives 5.9 g of

the expected product.

m. p.=148.degree. C.

EXAMPLE 196

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide hydrochloride

A saturated solution of gaseous HCl in ether is added dropwise to a solution of 5.9 g of the compound obtained above in 50 ml of ether until pH=1. The precipitate formed is filtered off, washed with ether and dried under vacuum to give 6.0 g of the expected hydrochloride. m.p.=224.degree. C. (dec.).

EXAMPLE 197

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide methanesulfonate

A solution of 0..062 g of methanesulfonic acid in 2 ml of acetone is added dropwise to a solution of 0.30 g of the compound obtained in example 195 in 3 ml of acetone. The white crystals formed upon cooling to 0.degree. C. are filtered off, washed with acetone and dried under vacuum to give 0.30 g of the expected salt. m.p.=218.degree. C.

EXAMPLE 198

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide hemifumarate

A solution of 0.038 g of fumaric acid in 6 ml of acetone is added dropwise to a solution of 0.30 g of the compound obtained in example 195 in 3 ml of acetone. The white crystals formed upon cooling to 0.degree. C. are filtered off, washed with acetone and dried under vacuum to give 0.23 g of the expected salt. m.p.=168.degree. C.

EXAMPLE 199

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide hydrogensulfate

0.018 ml of concentrated sulfuric acid are added to a solution of 0.30 g of the compound obtained in example 195 in 3 ml of acetone. The white crystals formed are filtered off, washed with acetone and then ether, and dried under vacuum to give 0.31 g of the expected salt. m.p.=240.degree. C.

EXAMPLE 200

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide paratoluenesulfonate

A solution of 0,123 g of paratoluenesulfonic acid in 6 ml of acetone is added dropwise to a solution of 0.30 g of the compound obtained in example 195 in 3 ml of acetone. The white crystals formed are filtered off, washed with acetone and dried under vacuum to give 0.34 g of the expected salt. m.p.=226.degree. C.

The compounds described in Table XX below are prepared by the procedure of example 1 (R.sub.4 .dbd.H) or example 153 (R.sub.4 .dbd.CH.sub.3)

TABLE XX

##STR307##

EXAMPLE	R.sub.4	R.sub.2	m.p.; .degree.C.
201	H	##STR308##	225
202	H	##STR309##	230
203	CH.sub.3	##STR310##	236
204	CH.sub.3	##STR311##	##STR312##
205	CH.sub.3	##STR313##	225
206	CH.sub.3	##STR314##	237
207	CH.sub.3	##STR315##	220
208	CH.sub.3	##STR316##	223

The preparation of 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxylic acid, already described in example 195, steps A-C, can be improved using for example the operating conditions described in examples 209 and 210 below:

EXAMPLE 209

5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxylic acid

A) Lithium salt of ethyl 4-(4-chlorophenyl)-3-methyl-4-oxydo-2-oxobuten-3-oate

2008 g of the lithium salt of hexamethyldisilazane are dissolved, in a reactor, under a nitrogen atmosphere, in 10.1 l of methylcyclohexane. A solution of 1686 g of 4-chloropropiophenone in 4 l of methylcyclohexane is then added slowly at 20.degree..+-.5.degree. C. After stirring for 4 and a half hours, 1607 g of ethyl oxalate are added over 35 minutes at 20.degree..+-.5.degree. C. The mixture is stirred for 17 hours at the same temperature. The solid formed is filtered off, washed with methylcyclohexane and dried under vacuum to give 1931 g of the expected product.

B) 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid

1/ 1921 g of the lithium salt obtained above are dissolved, in a reactor, under a nitrogen atmosphere, in 11 l of EtOH. 1493 g of 2,4-dichlorophenylhydrazine hydrochloride are then immediatly added at 20.degree..+-.5.degree. C. The mixture is stirred for 1 hour and 2.88 l of deionized water are then added, and stirring is continued for 17 hours at 20.degree..+-.5.degree. C. The precipitate formed is filtered off, washed with 80 % (v/v) ethanol and dried under vacuum to give 2280 g of the expected hydrazone. M.p.=140.degree. C.

2/ 2267 g of hydrazone are dissolved, in a reactor, under a nitrogen atmosphere, in 11.3 l of toluene. 201.6 g of paratoluenesulfonic acid are then added and the mixture is refluxed for 3 hours. The mixture is cooled to 20.degree..+-.5.degree. C. and paratoluenesulfonic acid is removed by extraction with deionized water. 120.75 g of benzyltriethylammonium chloride and then a solution of 636 g of NaOH in 1180 ml of deionized water are added to the toluene solution. The

mixture is heated for 4 hours at 68.degree..+-.3.degree. C. with vigorous stirring, sodium hydroxide is then neutralized and the reaction mixture is acidified with 1500 ml of HCl (d=1.19). The mixture is cooled to 20.degree..+-.5.degree. C., the precipitate formed is filtered off, washed with toluene and then deionized water, and dried under vacuum to give 1585 g of the expected product. M.p.=210.degree. C.

EXAMPLE 210

5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxylic acid

A) 1-(4-chlorophenyl)-1-trimethylsilyloxypropene

13.47 g of chlorotrimethylsilane are slowly added to 12.55 g of triethylamine, under a nitrogen atmosphere, at 20.degree..+-.3.degree. C. 16.86 g of 4-chloropropiophenone (endothermic mixture) and then a solution of 18.58 g of sodium iodide in 125 ml of acetonitrile are further added while maintaining the temperature at 18.degree..+-.2.degree. C. The mixture is then heated for 3 hours at 40.degree..+-.5.degree. C., the acetonitrile is removed under reduced pressure and 150 ml of toluene are added to the solid residue. 50 ml of solvent are distilled under reduced pressure to drive the residual acetonitrile off. The inorganic materials are extracted with 100 ml of iced water, the organic phase is washed with 100 ml of iced water and dried over magnesium sulfate. The toluene is removed under reduced pressure and complete removal of the solvents is performed for 15 hours at 60.degree. C. under a pressure of 1 mbar to give 22.7 g of an oil. NMR run at 200 MHz (CDCl.sub.3) 0.13 ppm:s:9H 1.7 ppm:d:3H 5.28 ppm:q:1H 7.21-7.39 ppm:m:4H.

B) Ethyl 3-(4-chlorobenzoyl)-3-methylpyruvate

10 g of anhydrous zinc chloride are suspended in 50 ml of toluene under a nitrogen atmosphere. Residual water is azeotropically driven off over 1 hour under atmospheric pressure. 20 ml of toluene and then 11.5 ml of ethyl ether are added to the mixture, cooled to 20.degree..+-.3.degree. C. A solution of 17 g of ethyl chloroglyoxylate diluted in 20 ml of dichloromethane is then slowly added to the mixture cooled to 0.degree..+-.2.degree. C. 14.5 g of the product obtained in the previous step are added over 1 and a half hours at the same temperature. The temperature is then allowed to rise to RT and the mixture is heated for 4 hours at 45.degree. C. The organic phase is washed with a solution of sodium hydrogen-carbonate and then water, and dried over magnesium sulfate. The solvents are removed under reduced pressure to give 17.6 g of an oil. NMR run at 200 MHz (CDCl.sub.3) 1.25 ppm:t:3H 1.35 ppm:d:3H 4.20 ppm:q:2H 4.93 ppm:q:1H 7.45-7.90 ppm m:4H.

C) Ethyl 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxylate

13.3 g of 2,4-dichlorophenylhydrazine hydrochloride are added to 17.6 g of the compound obtained in the previous step and the mixture is stirred for 18 hours at 20.degree..+-.3.degree. C. Without isolating the hydrazone, 0.56 g of paratoluenesulfonic acid are then added and the ternary azeotrope (water, ethanol, toluene) is distilled. Toluene reflux is continued for 1 hour and the reaction mixture is then cooled to 20.degree..+-.3.degree. C. The insoluble material is filtered off and the toluene solution is then washed twice with 100 ml of water. The solvents are removed under reduced pressure to give a crude oil which is used as such in the next step.

D) 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxylic acid

8.1 g of KOH in pellets are added to a solution of the oil obtained in the previous step in 100 ml of MeOH. The mixture is left for 1 hour at 25.degree..+-.3.degree. C. and the solvents are then removed under reduced pressure. The residue is taken up with 200 ml of water and 40 ml of toluene, the mixture is heated at 60.degree..+-.3.degree. C., decanted, and the aqueous phase is extracted three times, at this temperature, with 40 ml of toluene. Hydrochloric acid is then added to the aqueous phase until pH=1.5. The white crystals formed are filtered off, washed with water and then iso ether and dried under vaccum to give 9.9 g of the expected product. M.p.=210.degree. C.

The compound of example 195 can also be prepared using operating conditions which are industrially more accessible, as described in example 211 below:

EXAMPLE 211

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide

A suspension of 1568.6 g of the acid obtained in step B of example 209 in 14.1 l of methylcyclohexane is heated, under a nitrogen atmosphere, to 83.degree..+-.3.degree. C., and a solution of 554.5 g of thionyl chloride in 1.57 l of methylcyclohexane is added thereto. The mixture is stirred for 3 hours at 83.degree..+-.3.degree. C. and the temperature is then increased over 2 hours up to the reflux temperature of methylcyclohexane while removing the excess thionyl chloride by distillation. The mixture is cooled to 10.degree..+-.3.degree. C. and a solution of 452.9 g of 1-aminopiperidine and 457.5 g of triethylamine in 3.14 1 of THF is then slowly added. The mixture is stirred for 17 hours while allLowing the temperature to rise to 20.degree..+-.5.degree. C., and the organic phase is successively washed, at 20.degree..+-.5.degree. C., with deionized water and a 4% aqueous solution of acetic acid. The organic phase is then washed, at 70.degree..+-.3.degree. C., with a 1.5% solution of NaOH and then deionized water, and the THF and water are driven off by azeotropic distillation under atmospheric pressure. The mixture is allowed to cool to 20.degree..+-.5.degree. C. The expected product crystallises, the precipate formed is filtered off, washed with methylcyclohexane and dried under vaccum to give 1627 g of the title compound. DSC: endothermic peak centered at 155.5.degree. C.

EXAMPLE 212

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide (solvate with ethanol)

10 g of the compound obtained in example 195 are suspended in 60 ml of absolute ethanol and the mixture is refluxed until complete dissolution of the compound. The mixture is allowed to cool to 20.degree..+-.3.degree. C. and stirring is continued for 2 hours. The white crystals formed are filtered off, washed with ethanol and dried under vacuum to give 9.6 g of the expected product. DSC: endothermic peak centered at 102.7.degree. C. % calculated C: 56.5 H: 5.29 N: 10.98 % found C: 56.43 H: 5.41 N: 11.05.

EXAMPLE 213

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide hydrochloride (solvate with ethanol)

40 g of the compound obtained in example 196 are suspended in 400 ml of absolute ethanol. The mixture is heated to the boiling point until complete dissolution of the compound and then stirred for 20 hours while

progressively cooling it to 20.degree..+-.3.degree. C. The white crystals formed are filtered off, washed with ethanol and dried under vacuum to give 29.6 g of the expected product. DSC: broad endothermic peak (175.degree.-230.degree. C.) Thermogravimetry: weight loss:about 8.2% starting at 100.degree. C.

% calculated	C: 53.04	H: 5.16	N: 10.31
% found	C: 52.68	H: 5.23	N: 10.34.

EXAMPLE 214

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide methanesulfonate (hemisolvate with acetone)

3.84 g of methanesulfonic acid are added at 20.degree..+-.3.degree. C. to a solution of 18.55 g of the compound obtained in example 195 in 185 ml of acetone and the mixture is stirred for 20 hours at the same temperature. The white crystals formed are filtered off, washed with acetone and dried under vacuum to give 21.65 g of the expected product. DSC: melting, recrystallisation at about 175.degree. C. then melting at 191.5.degree. C. Thermogravimetry: weight less:about 5.2 % starting at 90.degree. C.

% calculated	C: 49.90	H: 4.75	N: 9.50
% found	C: 49.70	H: 4.76	N: 9.44.

EXAMPLE 215

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide paratoluenesulfonate

7.61 g of paratoluenesulfonic acid are added at 20.degree..+-.3.degree. C. to a solution of 18.55 g of the compound obtained in example 195 in 185 ml of acetone and the mixture is stirred for 20 hours at the same temperature. The white crystals formed are filtered off, washed with acetone and dried under vacuum to give 24.25 g of the expected product. DSC: endothermic peak centered at 236.8.degree. C.

% calculated	C: 54.16	H: 4.60	N: 8.72
% found	C: 54.11	H: 4.71	N: 8.69.

EXAMPLE 216

N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide dihydrogenphosphate

4.61 g of 85% phosphoric acid are added at 20.degree..+-.3.degree. C. to a solution of 18.55 g of the compound obtained in example 195 in 185 ml of methylethylketone. Water is removed by distillation under atmospheric pressure of the azeotrope methylethylketone/water. The mixture is progressively cooled to 20.degree..+-.3.degree. C. while stirring for 20 hours. The white crystals formed are filtered off, washed with methylethylketone and dried under vacuum to give 21 g of the expected product. DSC: endothermic peak centered at 185.5.degree. C.

% calculated	C: 47.04	H: 4.31	N: 9.97
% found	C: 46.96	H: 4.62	N: 9.98.

CLM What is claimed is:

1. A compound of the formula ##STR317## in which g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 are identical or different and are independently hydrogen, a chlorine or bromine atom, a (C.sub.1 -C.sub.3)-alkyl, a (C.sub.1 -C.sub.3)-alkoxy, a trifluoromethyl or a nitro group and g.sub.4 is optionally a phenyl group; R.sub.4 is hydrogen or a (C.sub.1 -C.sub.3)-alkyl; X is either a direct bond or a group --(CH.sub.2).sub.x --N(R.sub.3)--, in which R.sub.3 is hydrogen or a (C.sub.1 -C.sub.3)-alkyl and x is zero or one; and, R is a group --NR.sub.1 R.sub.2 in which R.sub.1 and R.sub.2 are independently a (C.sub.1 -C.sub.6)-alkyl; an optionally-substituted non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical; an amino (C.sub.1 -C.sub.4) alkyl group in which the amino is optionally disubstituted by a (C.sub.1 -C.sub.3)-alkyl; a cycloalkyl-(C.sub.1 -C.sub.3) alkyl in which the cycloalkyl is C.sub.3 -C.sub.12 ; a phenyl which is unsubstituted or monosubstituted or polysubstituted by a halogen, by a (C.sub.1 -C.sub.5)-alkyl or by a (C.sub.1 -C.sub.5)-alkoxy; a phenyl (C.sub.1 -C.sub.3)-alkyl; a diphenyl-(C.sub.1 -C.sub.3)-alkyl; a naphthyl; an anthracenyl; a saturated 5- to 8-membered heterocyclic radical which is unsubstituted or substituted by a (C.sub.1 -C.sub.3)- alkyl, by a hydroxyl or by a benzyl group; a 1-adamantylmethyl; an aromatic heterocycle unsubstituted, mono- or polysubstituted by a halogen, a (C.sub.1 -C.sub.5)-alkyl, a (C.sub.1 -C.sub.5)-alkoxy; a (C.sub.1 -C.sub.3)-alkyl substituted by an aromatic heterocycle unsubstituted or mono- or polysubstituted by a halogen, a (C.sub.1 -C.sub.5) alkyl, a (C.sub.1 -C.sub.5)-alkoxy, or else R.sub.1 is hydrogen and R.sub.2 is as defined above, or else R.sub.1 and R.sub.2, together with the nitrogen atom to which they are bonded,form a saturated 5- to 8-membered heterocyclic radical, said heterocyclic radical being other than morpholine when w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 are all hydrogen; a group R.sub.2 as defined above when X is --(CH.sub.2).sub.x N(R.sub.3)--; or a group R.sub.5 when X is a direct bond, R.sub.5 being a (C.sub.1 -C.sub.3)-alkyl; a (C.sub.3 -C.sub.12)-cycloalkyl which is unsubstituted or substituted by a (C.sub.1 -C.sub.5)-alkyl; a phenyl-(C.sub.1 -C.sub.3)-alkyl which is unsubstituted or substituted by a halogen or by a (C.sub.1 -C.sub.5)-alkyl; a cycloalkyl-(C.sub.1 -C.sub.3)-alkyl in which the cycloalkyl is C.sub.3 -C.sub.12 and is unsubstituted or substituted by a (C.sub.1 -C.sub.5)-alkyl; or a 2-norbornylmethyl; or one of its salts.

2. A compound according to claim 1 of the formula ##STR318## in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 are as defined for (I) in claim 1, R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl and R.sub.2 is a non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical or a saturated 5- to 8-membered heterocyclic radical selected from 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, 4-morpholinyl and 4-thiomorpholinyl, or one of its salts.

3. A compound according to claim 1 of the formula ##STR319## in which R.sub.4, X and R are as defined for (I) in claim 1, or one of its salts.

4. A compound of formula (i) according to claim 3 in which R.sub.4 is hydrogen or a methyl group, or one of its salts.

5. A compound of formula (i) according to claim 3 in which R.sub.4 is hydrogen or methyl and X is a direct bond, or one of its salts.

6. A compound of formula (i) according to claim 3 in which R.sub.4 is hydrogen or methyl, X is a direct bond and R is a group --NR.sub.1

R.sub.2 in which R.sub.1 is hydrogen or a methyl group and R.sub.2 is a non-aromatic C.sub.3 -C.sub.15 carbocyclic radical or a saturated 5- to 8-membered heterocyclic radical selected from 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, 4-morpholinyl and 4-thiomorpholinyl, or one of its salts.

7. A compound which is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide, or one of its salts or solvates thereof.

8. A compound according to claim 7 wherein said salts or solvates are selected from the group consisting of the hydrochloride or its solvate with ethanol, the methanesulfonate or its hemisolvate with acetone, the hemifumarate, the hydrogensulfate, the paratoluenesulfonate and the dihydrogenphosphate.

9. A compound of formula (i) according to claim 3 in which R.sub.4 is hydrogen or methyl, X is --(CH.sub.2).sub.x --N(R.sub.3)-- and R is --NR.sub.1 R.sub.2, x is zero or one, R.sub.3 is hydrogen or a methyl group, R.sub.1 is hydrogen and R.sub.2 is a phenyl which is unsubstituted or substituted by one or two halogen atoms, a (C.sub.1 -C.sub.5)-alkyl group or a (C.sub.1 -C.sub.5)-alkoxy group, or a non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical, or one of its salts.

10. A compound according to claim 1 of the formula ##STR320## in which X and R are as defined for (I) in claim 1 and w.sub.4 is a methyl group or a methoxy group, or one of its salts.

11. A compound of formula (ii) according to claim 10 in which w.sub.4 is methyl or methoxy, X is a direct bond and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a methyl group and R.sub.2 is a non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical, or one of its salts.

12. A compound of formula (ii) according to claim 10 in which w.sub.4 is methyl or methoxy, X is a group --(CH.sub.2).sub.x --N(R.sub.3)-- in which x is zero or one and R.sub.3 is hydrogen or a methyl group, and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen and R.sub.2 is a phenyl which is unsubstituted or substituted by one or two halogen atoms, a (C.sub.1 -C.sub.5)-alkyl group or a (C.sub.1 -C.sub.5)-alkoxy group, or a non-aromatic (C.sub.3 -C.sub.15) carbocyclic radical, or one of its salts.

13. A compound of formula (I) according to claim 1 in which w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6, g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and R.sub.4 and X are as defined for (I) in claim 1 and R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl group and R.sub.2 is a 2- or 3-indolyl-(C.sub.1 -C.sub.3)-alkyl group or a 2- or 3-indolyl group, or one of its salts.

14. A compound according to claim 1 of the formula ##STR321## in which X is as defined for (I) in claim 1, R is a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen or a (C.sub.1 -C.sub.6)-alkyl and R.sub.2 is a 2- or 3-indolyl-(C.sub.1 -C.sub.3)-alkyl group or a 2or 3-indolyl group, and either w.sub.2 is hydrogen and w.sub.4 is a methyl or methoxy group or w.sub.2 and w.sub.4 are a chlorine atom, or one of its salts.

15. A compound according to claim 1 of the formula ##STR322## in which X and R are as defined for (I) in claim 1 and g.sub.4 is a bromine atom or a methyl or trifluoromethyl group, or one of its salts.

16. A compound of the formula ##STR323## in which R.sub.4 is as defined for (I) in claim 1 and Alk is a (C.sub.1 -C.sub.5)-alkyl.

17. A pharmaceutical composition containing a pharmaceutically effective amount of a compound of formula (I) according to claim 1 or one of its pharmaceutically acceptable salts, mixed with at least one pharmaceutically acceptable excipient.

18. A pharmaceutical composition according to claim 17, which is in the form of a dosage unit.

19. A pharmaceutical composition according to claim 18, containing from 0.5 to 1000 mg of active principle.

20. A pharmaceutical composition according to claim 17, wherein the active principle is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-pyrazole-3-carboxamide, or one of its pharmaceutically acceptable salts or solvates thereof.

21. A compound according to claim 1, wherein: g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 and w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 are identical or different and are independently hydrogen, a chlorine or bromine atom, a (C.sub.1 -C.sub.3)alkyl, a (C.sub.1 -C.sub.3)alkoxy, a trifluoromethyl or a nitro group and g.sub.4 is optionally a phenyl group; R.sub.4 is hydrogen or a (C.sub.1 -C.sub.3)alkyl; and either: (a) X is a direct bond, and R is: (i) a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen; a (C.sub.1 -C.sub.5)alkyl or a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical and R.sub.2 is a (C.sub.1 -C.sub.6)alkyl; a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical optionally substituted by at least a (C.sub.1 -C.sub.5)alkyl, a (C.sub.1 -C.sub.5)alkoxy, a halogen and/or a hydroxy; an amino(C.sub.1 -C.sub.4)alkyl group in which the amino is disubstituted by a (C.sub.1 -C.sub.3)alkyl; a (C.sub.3 -C.sub.12)cycloalkyl(C.sub.1 -C.sub.3)alkyl; a phenyl which is unsubstituted or monosubstituted by a halogen or a (C.sub.1 -C.sub.5)alkyl; a phenyl(C.sub.1 -C.sub.3)alkyl; a diphenyl(C.sub.1 -C.sub.3)alkyl; a saturated 5- to 8-membered heterocyclic radical selected from the group consisting of pyrrolidinyl, piperidyl, morpholinyl, hexahydroazepinyl, quinuclidinyl, oxabicycloheptanyl, azabicyclo[2.2.1]heptanyl and azabicyclo[2.2.2]octanyl, unsubstituted or substituted by a (C.sub.1 -C.sub.3)alkyl or a benzyl group; or a (C.sub.1 -C.sub.3)alkyl substituted by an aromatic heterocycle selected from the group consisting of pyrrolyl, pyridyl and indolyl, unsubstituted or monosubstituted by a (C.sub.1 -C.sub.5)alkyl; or else R.sub.1 and R.sub.2, together with the nitrogen atom to which they are bonded, form a saturated 5- to 8-membered heterocyclic radical selected from the group consisting of pyrrolidinyl, piperidyl and morpholinyl, said heterocyclic radical being other than morpholine when w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 are all hydrogen; or (ii) a group R.sub.5, R.sub.5 being a phenyl(C.sub.1 -C.sub.3)alkyl in which the phenyl is substituted by a (C.sub.1 -C.sub.5)alkyl; a (C.sub.3 -C.sub.12)cycloalkyl(C.sub.1 -C.sub.3)alkyl; or a 2-norbornylmethyl; or (b) X is a group --(CH.sub.2).sub.x --N(R.sub.3)-- in which R.sub.3 is hydrogen or a (C.sub.1 -C.sub.3)alkyl and x is zero or one and R is: (i) a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen and R.sub.2 is a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical or a phenyl which is unsubstituted or mono- or disubstituted by a halogen, a (C.sub.1 -C.sub.5)alkyl or a (C.sub.1 -C.sub.5)alkoxy; or (ii) a group R.sub.2, R.sub.2 being a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical; a phenyl substituted by a halogen; an anthracenyl; or an indolyl optionally substituted by a (C.sub.1 -C.sub.5)alkoxy; or one, of its salts.

22. A compound according to claim 1, wherein X is a direct bond and R represents: (i) a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen;

a (C.sub.1 -C.sub.6)alkyl or a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical and R.sub.2 is a (C.sub.1 -C.sub.6)alkyl; a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical optionally substituted by at least a (C.sub.1 -C.sub.5)alkyl, a (C.sub.1 -C.sub.5)alkoxy, a halogen and/or a hydroxy; an amino(C.sub.1 -C.sub.4)alkyl group in which the amino is disubstituted by a (C.sub.1 -C.sub.3)alkyl; a (C.sub.3 -C.sub.12)cycloalkyl(C.sub.1 -C.sub.3)alkyl; a phenyl which is unsubstituted or monosubstituted by a halogen or a (C.sub.1 -C.sub.5)alkyl; a phenyl(C.sub.1 -C.sub.3)alkyl; or a diphenyl(C.sub.1 -C.sub.3)alkyl; or (ii) a group R.sub.5, R.sub.5 being a phenyl(C.sub.1 -C.sub.3)alkyl in which the phenyl is substituted by a (C.sub.1 -C.sub.5)alkyl; a (C.sub.3 -C.sub.12)cycloalkyl(C.sub.1 -C.sub.3)alkyl; or a 2-norbornylmethyl; or one of its salts.

23. A compound according to claim 1, wherein X is a direct bond and R represents a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen; a (C.sub.1 -C.sub.6)alkyl or a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical and R.sub.2 is a saturated 5- to 8-membered heterocyclic radical selected from the group consisting of pyrrolidinyl, piperidyl, morpholinyl, hexahydroazepinyl, quinuclidinyl, oxabicycloheptanyl, azabicyclo[2.2.1]heptanyl and azabicyclo[2.2.2]octanyl, unsubstituted or substituted by a (C.sub.1 -C.sub.3)alkyl or a benzyl group; or else R.sub.1 and R.sub.2, together with the nitrogen atom to which they are bonded, form a saturated 5- to 8-membered heterocyclic radical selected from the group consisting of pyrrolidinyl, piperidyl and morpholinyl, said heterocyclic radical being other than morpholine when w.sub.2, w.sub.3, w.sub.4, w.sub.5 and w.sub.6 and g.sub.2, g.sub.3, g.sub.4, g.sub.5 and g.sub.6 are all hydrogen; or one of its salts.

24. A compound according to claim 1, wherein X is a direct bond and R represents a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen; a (C.sub.1 -C.sub.6)alkyl or a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical and R.sub.2 is a (C.sub.1 -C.sub.3)alkyl substituted by an aromatic heterocycle selected from the group consisting of pyrrolyl, pyridyl and indolyl, unsubstituted or monosubstituted by a (C.sub.1 -C.sub.5)alkyl; or one of its salts.

25. A compound according to claim 1, wherein X is a group --(CH.sub.2).sub.x --N(R.sub.3)-- in which R.sub.3 is hydrogen or a (C.sub.1 -C.sub.3)alkyl and x is zero or one and R is: (i) a group --NR.sub.1 R.sub.2 in which R.sub.1 is hydrogen and R.sub.2 is a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical or a phenyl which is unsubstituted or mono- or disubstituted by a halogen, a (C.sub.1 -C.sub.5)alkyl or a (C.sub.1 -C.sub.5)alkoxy; or (ii) a group R.sub.2, R.sub.2 being a non-aromatic (C.sub.3 -C.sub.15)carbocyclic radical; a phenyl substituted by a halogen; an anthracenyl; or an indolyl optionally substituted by a (C.sub.1 -C.sub.5)alkoxy; or one of its salts.

26. A pharmaceutical composition according to claim 18, wherein the active principiple is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, or one of its pharmaceutically acceptable salts or a solvate thereof.

27. A pharmaceutical composition according to claim 19, wherein the active principle is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, or one of its pharmaceutically acceptable salts or a solvate thereof.

28. A pharmaceutical composition containing a pharmaceutically effective amount of a compound of formula (I) according to claim 1, or one of its pharmaceutically acceptable salts, mixed with at least one pharmaceutically acceptable excipient.

29. A pharmaceutical composition according to claim 29 which is in the form of a dosage unit.

30. A pharmaceutical composition according to claim 29 containing from 0.5 to 1000 mg of active principle.

INCL INCLM: 514/326.000
INCLS: 514/212.000; 514/236.500; 514/341.000; 514/404.000; 514/406.000; 514/407.000; 544/127.000; 546/247.000; 546/211.000; 548/357.500; 548/364.100; 548/364.700; 548/371.700; 548/372.500; 548/374.100; 548/375.100
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NCLS: 514/217.090; 514/236.500; 514/341.000; 514/404.000; 514/406.000; 514/407.000; 544/127.000; 546/211.000; 546/247.000; 548/357.500; 548/364.100; 548/364.700; 548/371.700; 548/372.500; 548/374.100; 548/375.100
IC [6]
ICM: A61K031-445
EXF 546/211; 546/247; 548/374.1; 548/364.4; 548/357.5; 548/364.1; 548/364.7; 548/375.1; 548/371.7; 548/372.5; 544/127; 514/212; 514/236.5; 514/326; 514/341; 514/404; 514/406; 514/407
ARTU 129
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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     FILE 'STNGUIDE' ENTERED AT 10:46:56 ON 30 MAY 2003

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L3             1 S US5624941/PN
L4             1 S L3 AND L1
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EP0255415 (IV)

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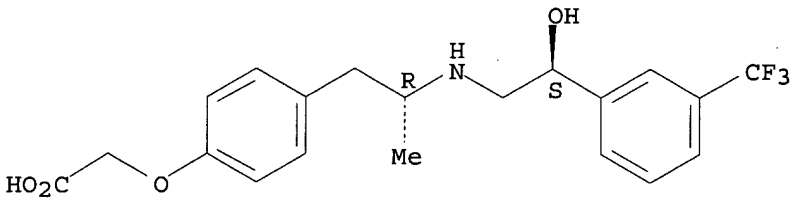
RN **118104-64-6** REGISTRY

Relative stereochemistry.

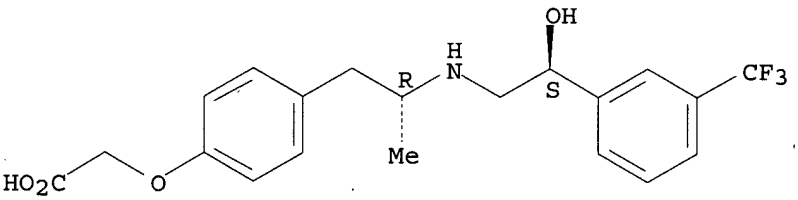


● HCl

=> d rn str l3 1-20

L3 ANSWER 1 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118104-64-6** REGISTRY

Relative stereochemistry.



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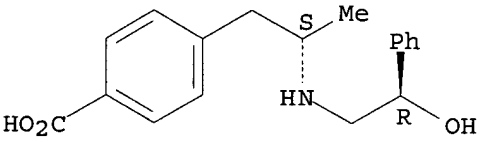
L3 ANSWER 2 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-25-8** REGISTRY

Relative stereochemistry.



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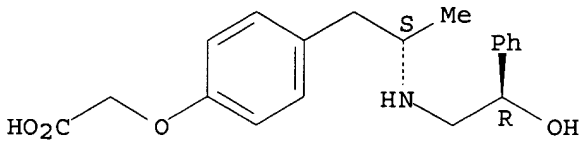
L3 ANSWER 3 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-24-7** REGISTRY

Relative stereochemistry.



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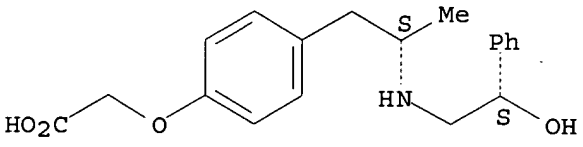
L3 ANSWER 4 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-23-6** REGISTRY

Relative stereochemistry.



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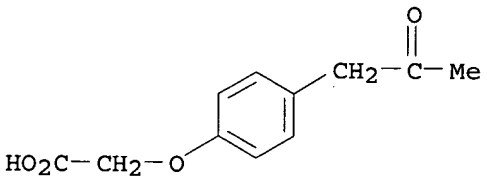
L3 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-22-5** REGISTRY



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L3 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-21-4** REGISTRY

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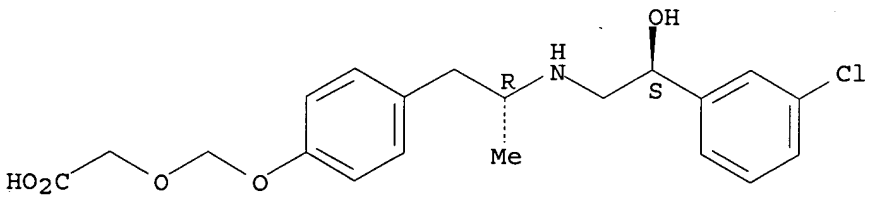
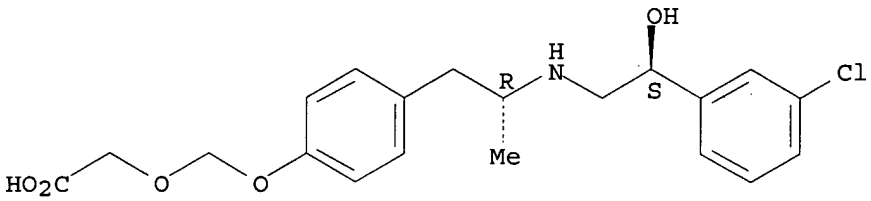


HBr

L3 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-20-3** REGISTRY

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 8 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-19-0** REGISTRY

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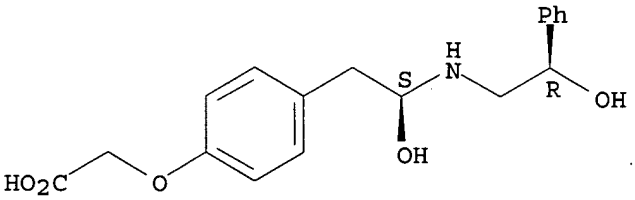

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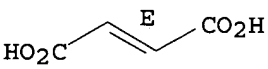

L3 ANSWER 9 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-17-8** REGISTRY

CM 1

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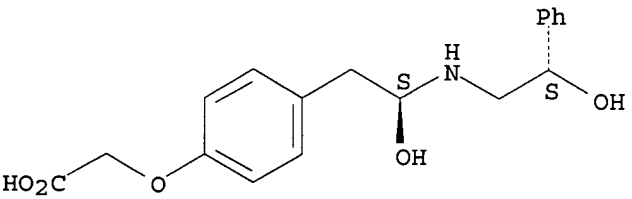
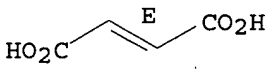
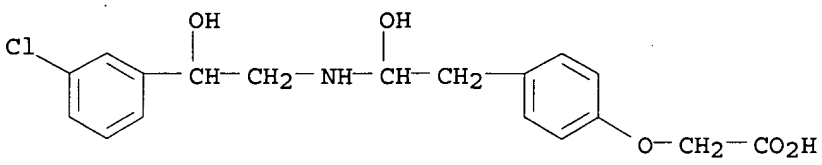


CM 2

Double bond geometry as shown.



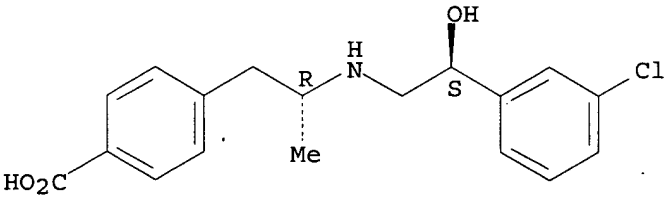
L3 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-15-6** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 11 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-14-5** REGISTRY

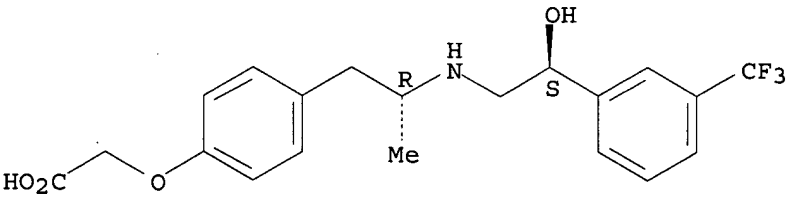
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

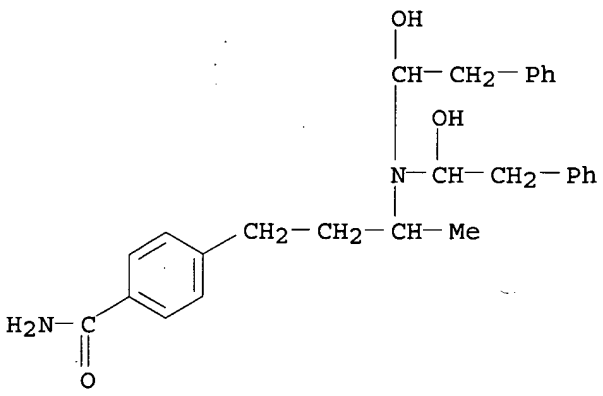
L3 ANSWER 12 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-13-4** REGISTRY

Relative stereochemistry.



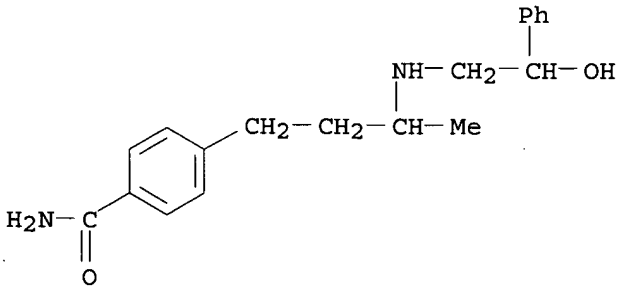
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 13 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-12-3** REGISTRY



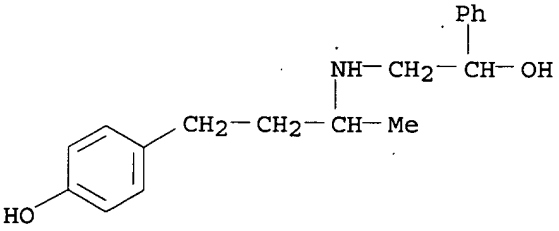
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 14 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-11-2** REGISTRY



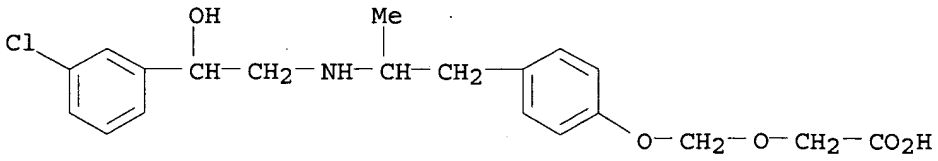
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 15 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-10-1** REGISTRY



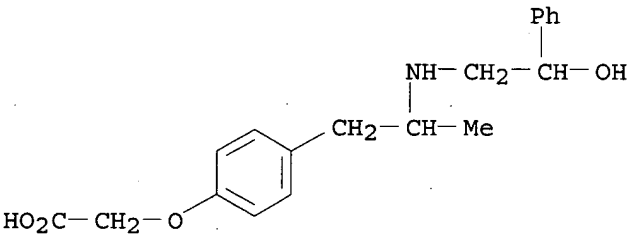
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 16 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **114333-70-9** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

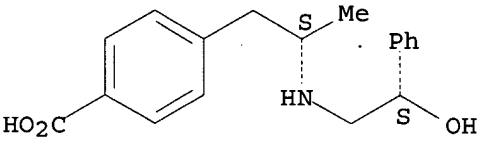
L3 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **114333-68-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

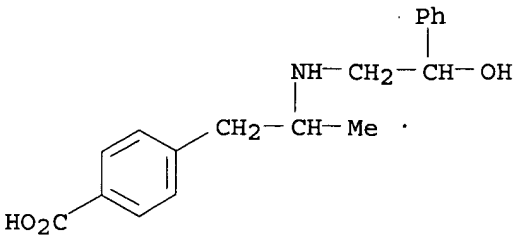
L3 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN 90730-94-2 REGISTRY

Relative stereochemistry.



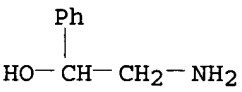
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **74733-64-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **7568-93-6** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L3 ANSWER 1 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118104-64-6** REGISTRY

L3 ANSWER 2 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-25-8** REGISTRY

L3 ANSWER 3 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-24-7** REGISTRY

L3 ANSWER 4 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-23-6** REGISTRY

L3 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-22-5** REGISTRY

L3 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-21-4** REGISTRY

L3 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-20-3** REGISTRY

L3 ANSWER 8 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-19-0** REGISTRY

L3 ANSWER 9 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-17-8** REGISTRY

L3 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-15-6** REGISTRY

L3 ANSWER 11 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-14-5** REGISTRY

L3 ANSWER 12 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-13-4** REGISTRY

L3 ANSWER 13 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-12-3** REGISTRY

L3 ANSWER 14 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-11-2** REGISTRY

L3 ANSWER 15 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **118076-10-1** REGISTRY

L3 ANSWER 16 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **114333-70-9** REGISTRY

L3 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **114333-68-5** REGISTRY

L3 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN 90730-94-2 REGISTRY

L3 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **74733-64-5** REGISTRY

L3 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2003 ACS
RN **7568-93-6** REGISTRY

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L13 ANSWER 1 OF 23 USPATFULL
AB This invention relates to new propanolamine derivatives or salts thereof
represented by the following formula [I]: ##STR1##

Wherein each symbol is as defined in the specification or salts thereof which have gut selective sympathomimetic, anti-ulcerous, anti-pancreatitis, lipolytic, anti-urinary incontinence and anti-pollakiuria activities, to processes for the preparation thereof, to a pharmaceutical composition comprising the same and to a method for the prevention and/or treatment diseases indicated in the specification to a human being or an animal.
AN 2002:222002 USPATFULL
TI Propanolamine derivatives
IN Taniguchi, Kiyoshi, Hyogo, JAPAN
Sakurai, Minoru, Osaka, JAPAN
Fujii, Naoaki, Osaka, JAPAN
Hosoi, Kumi, Shizuoka, JAPAN
Tomishima, Yasuyo, Osaka, JAPAN
Takasugi, Hisashi, Osaka, JAPAN
Sogabe, Hajime, Tokyo, JAPAN
Ishikawa, Hirofumi, Osaka, JAPAN
Hanioka, Naomi, Osaka, JAPAN
PA Fujisawa Pharmaceutical Co. Ltd., Osaka-shi, JAPAN (non-U.S. corporation)
PI US 2002120148 A1 20020829
AI US 2002-74020 A1 20020214 (10)
RLI Continuation of Ser. No. US 2000-646878, filed on 22 Nov 2000, PENDING
PRAI WO 1999-JP1500 19990325
AU 1998-2826 19980406
AU 1998-5058 19980804
DT Utility
FS APPLICATION
LREP OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 116049-79-7 **121524-09-2** 173901-95-6 193759-91-0
246262-41-9
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

L13 ANSWER 2 OF 23 USPATFULL
AB The present invention provides methods of treating non-insulin dependent
diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose
tolerance, the methods comprising the step of administering to a patient
having or at risk of having non-insulin dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic

ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance a synergistic amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel blocker; and 2) a cAMP phosphodiesterase type 3 inhibitor. The present invention also provides kits and pharmaceutical compositions that comprise: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel blocker; and 2) a cAMP phosphodiesterase type 3 inhibitor. The present invention also relates to kits and pharmaceutical compositions that comprise 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel blocker; 2) a cAMP phosphodiesterase type 3 inhibitor; and 3) an additional compound useful for the treatment of non-insulin dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance.

AN 2002:22432 USPATFULL

TI Synergistic effect of a sulfonylurea and/or non-sulfonylurea Kchannel blocker, and a phosphodiesterase 3 type inhibitor

IN Fryburg, David A., East Lyme, CT, UNITED STATES
Parker, Janice C., Ledyard, CT, UNITED STATES

PI US 2002013268 A1 20020131
AI US 2001-829874 A1 20010410 (9)
PRAI US 2000-196728P 20000413 (60)
DT Utility
FS APPLICATION
LREP Gregg C. Benson, Pfizer Inc., Patent Department, MS 4159, Eastern Point Road, Groton, CT, 06340
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 1475

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin 458-24-2, Fenfluramine 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 7440-62-2D, Vanadium, complexes 9004-10-8D, Insulin, analogs 10238-21-8, Glyburide 21187-98-4, Gliclazide 23602-78-0, Benfluorex 28299-33-4D, Imidazoline, derivs. 29094-61-9, Glipizide 37353-31-4, Vanadate 51037-30-0, Acipimox 56180-94-0, Acarbose 60719-84-8, Amrinone 66529-17-7, Midaglizole 68550-75-4, Cilostamide 72432-03-2, Miglitol 73384-60-8 73963-72-1, Cilostazol 74150-27-9, Pimobendan 74772-77-3, Ciglitazone 75358-37-1, Linogliride 77671-31-9, Enoximone 78415-72-2, Milrinone 79944-58-4, Idazoxan 80879-63-6, Emiglitate 81840-15-5, Vesnarinone 83480-29-9, Voglibose 84243-58-3, Imazodan **86615-96-5**, BRL 35135 88431-47-4, Clomoxir 89197-32-0, Efaroxan 90505-66-1, Ro 16-8714 90730-96-4, BRL 37344 93479-97-1, Glimepiride 94192-59-3, Lixazinone 97322-87-7, Troglitazone 100510-33-6, Adibendan 100643-96-7, Indolidan 102669-89-6, Saterinone 104343-33-1, MDL-25637 105182-45-4, Fluparoxan 105816-04-4, Nateglinide 106612-94-6, Insulinotropin (human) 107444-51-9 109229-58-5, Englitazone 110605-64-6, Isaglidole 111025-46-8, Pioglitazone 112018-01-6, Bemoradan 115344-47-3, Siguazodan 122320-73-4, Rosiglitazone

122575-28-4, Naglivan 122830-14-2, Deriglidole 124083-20-1, Etomoxir
127214-23-7, Camiglibose **129689-30-1**, ICI D7114 130714-47-5,
WAG 994 133107-64-9 135062-02-1, Repaglinide **138908-40-4**,
CL316243 141200-24-0, Darglitazone 187887-46-3, Symlin
335149-21-8,
AC2993
(sulfonylurea and/or non-sulfonylurea K+ ATP channel blocker and phosphodiesterase 3 type inhibitor synergism for treatment of non-insulin-dependent diabetes or other conditions)

L13 ANSWER 3 OF 23 USPATFULL
AB A method and system for forwarding data-packets in a data-over-cable system, is provided. The data-packets received by the head-end of the data-over-cable system are sorted according to the Quality-of-Service identifiers assigned to the destination for the respective data-packets.
The sorted data-packets are forwarded subsequently in accordance with the Quality-of-Service settings corresponding to their respective Quality-of-Service identifiers. Data-packets that cannot be transmitted in accordance with their respective Quality-of-Service identifiers are cached for transmission at a later time point.
AN 2002:218126 USPATFULL
TI Method and system for quality-of-service based data forwarding in a data-over-cable system
IN Beser, Nurettin B., Evanston, IL, United States
PA 3Com Corporation, Santa Clara, CA, United States (U.S. corporation)
PI US 6442158 B1 20020827
AI US 1998-85736 19980527 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Olms, Douglas; Assistant Examiner: Sam, Phirin
LREP McDonnell Boehnen Hulbert & Berghoff
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1135
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 74513-77-2, RO363 74772-77-3, Ciglitazone 97322-87-7, Troglitazone
109229-58-5, Englitazone 111025-46-8, Pioglitazone 122320-73-4,
BRL49653 **138908-40-4**, CL316243
(effect of, in adipocytes; IR thermog. for measuring real-time thermogenesis in organisms and cells)

L13 ANSWER 4 OF 23 USPATFULL
AB A method of reducing cravings in a mammal to food or an addictive substance is disclosed. The method comprises administering to the mammal
an effective amount of a D.sub.1/D.sub.5 antagonist or a D.sub.1/D.sub.5
partial agonist alone or in combination with other specified CNS compounds.
AN 2001:165828 USPATFULL
TI Method of reducing craving in mammals
IN Coffin, Vicki L., Basking Ridge, NJ, United States
Glue, Paul W., Flemington, NJ, United States
PI US 2001025038 A1 20010927
AI US 2001-846170 A1 20010501 (9)
RLI Division of Ser. No. US 1998-178447, filed on 23 Oct 1998, PENDING
PRAI US 1997-64563P 19971028 (60)

DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 594
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 34911-55-2, Bupropion 36505-84-7, Buspirone 58939-37-0, A 69024 67287-49-4, SKF 38393 87134-87-0, Sch 23390 maleate **121524-09-2** , SR 58611a 150490-85-0, NNC-22-0010 171285-42-0, JHS 136 171285-53-3, JHS 271 175413-88-4, JHS 198 190133-94-9, SCH 39166 193480-75-0 224031-15-6, BTS-73-947
(method of reducing nicotine and tobacco craving in mammals)

L13 ANSWER 5 OF 23 USPATFULL
AB A method of reducing cravings in a mammal to nicotine or tobacco is disclosed. The method comprises administering to the mammal an effective amount of a D.sub.1 /D.sub.5 antagonist or a D.sub.1 /D.sub.5 partial agonist alone or in combination with other specified CNS compounds.
AN 2001:112314 USPATFULL
TI Method of reducing nicotine and tobacco craving in mammals
IN Coffin, Vicki L., Basking Ridge, NJ, United States
Glue, Paul W., Flemington, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 6262049 B1 20010717
AI US 1998-178447 19981023 (9)
PRAI US 1997-64563P 19971028 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Mazer, Edward H.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 570
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 34911-55-2, Bupropion 36505-84-7, Buspirone 58939-37-0, A 69024 67287-49-4, SKF 38393 87134-87-0, Sch 23390 maleate **121524-09-2** , SR 58611a 150490-85-0, NNC-22-0010 171285-42-0, JHS 136 171285-53-3, JHS 271 175413-88-4, JHS 198 190133-94-9, SCH 39166 193480-75-0 224031-15-6, BTS-73-947
(method of reducing nicotine and tobacco craving in mammals)

L13 ANSWER 6 OF 23 USPATFULL
AB The present invention provides a method of reducing a wasting condition, which can occur due to a pathology or to a particular physiologic or metabolic state in a subject, by administering to the subject a substituted 1,3-benzodioxole.
AN 97:7947 USPATFULL
TI Use of a substituted 1,3-benzodioxole to reduce a wasting condition
IN Girten, Beverly E., San Diego, CA, United States
Tuttle, Ronald R., Escondido, CA, United States
PA Houghten Pharmaceuticals, San Diego, CA, United States (U.S. corporation)
PI US 5597843 19970128

AI US 1995-485609 19950607 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Henley, III, Raymond
LREP Campbell & Flores LLP
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 459
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 274-09-9D, 1,3-Benzodioxole, derivs. **138908-40-4**, HP 186
(substituted benzodioxole to reduce wasting condition)

L13 ANSWER 7 OF 23 USPATFULL
AB Substituted 5-2-((2-aryl-2-hydroxyethyl)amino)propyl)-1,3-benzodioxoles having the structural formula: ##STR1## wherein R4, R5, R6, R7, and R8 are as hereinafter defined, are .beta.3-adrenergic agonists useful in the treatment of elevated intraocular pressure and glaucoma.
AN 96:92089 USPATFULL
TI Treatment of glaucoma and ocular hypertension with .beta.3-adrenergic agonists
IN Brazzell, Romulus K., New City, NY, United States
Dubnick, Bernard, Westwood, NJ, United States
PA American Cyanamid Company, Wayne, NJ, United States (U.S. corporation)
PI US 5563171 19961008
AI US 1993-148153 19931105 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Cintins, Marianne M.; Assistant Examiner: MacMillan, Keith
LREP Hedman, Gibson & Costigan
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 541
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **138908-40-4** 139012-91-2 139013-02-8 139013-03-9
143485-19-2 183720-02-7
(benzodioxole deriv. .beta.3-adrenergic agonists for treatment of glaucoma)

L13 ANSWER 8 OF 23 USPATFULL
AB A method for the enantioselective reduction of an .alpha.-iminoketone to
an .alpha.-aminoalcohol is disclosed. The method utilizes a borane reducing agent as the reducing agent and a chiral 1,3,2-oxazaborole as the catalyst. The method is applied to the synthesis of R-albuterol from
methyl 5-acetylsalicylate in high yield and high optical purity.
AN 95:73798 USPATFULL
TI Asymmetric synthesis of (R)- and (S)-arylethanolamines from iminoketones
IN Gao, Yun, Southborough, MA, United States
Hong, Yaping, Worcester, MA, United States
Zepp, Charles M., Berlin, MA, United States
PA Sepracor, Inc., Marlborough, MA, United States (U.S. corporation)
PI US 5442118 19950815
AI US 1994-231231 19940422 (8)
DT Utility

FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
LREP Heslin & Rothenberg
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 479
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 586-06-1DP, Metaproterenol, enantiomer 3930-20-9DP, Sotalol, enantiomer
7683-59-2DP, Isoproterenol, enantiomer 23031-25-6DP, Terbutaline, enantiomer 36894-69-6DP, Labetalol, enantiomer **86615-96-5DP**, BRL 35135, enantiomer 90730-96-4DP, BRL 37344, enantiomer **138908-40-4P**, CL 316243
(asym. synthesis of (R)- and (S)-arylethanolamines from imino ketones using chiral 1,3,2-oxazaborole catalysts)

L13 ANSWER 9 OF 23 USPATFULL
AB The present invention discloses substituted 1,3-benzodioxoles which possess anti-diabetic and/or anti-hyperglycemic and/or anti-obesity properties in humans and other animals.
AN 94:108943 USPATFULL
TI Substituted
5-(2-((2-aryl-2-hydroxyethyl)amino)propyl)-1,3-benzodioxoles
IN Bloom, Jonathan D., Hartsdale, NY, United States
Claus, Thomas H., Montvale, NJ, United States
DeVries, Vern G., Ridgewood, NJ, United States
Dolan, Jo A., Spring Valley, NY, United States
Dutia, Minu D., West Nyack, NY, United States
PA American Cyanamid Company, Wayne, NJ, United States (U.S. corporation)
PI US 5373020 19941213
AI US 1993-71443 19930603 (8)
RLI Division of Ser. No. US 1992-896319, filed on 10 Jun 1992, now patented,
Pat. No. US 5245053 which is a division of Ser. No. US 1991-742409, filed on 8 Aug 1991, now patented, Pat. No. US 5151439 which is a division of Ser. No. US 1990-519192, filed on 4 May 1990, now patented, Pat. No. US 5061727
DT Utility
FS Granted
EXNAM Primary Examiner: Daus, Donald G.
LREP Costigan, James V., Jackson, H. G.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1483
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138908-34-6P 138908-35-7P 138908-36-8P 138908-37-9P 138908-38-0P
138908-39-1P **138908-40-4P** 138908-41-5P 138908-42-6P
138908-43-7P 138908-44-8P 138908-45-9P 138908-46-0P 138908-52-8P
138908-54-0P 138908-59-5P 138908-60-8P 139012-91-2P 139012-92-3P
139012-93-4P 139012-94-5P 139012-95-6P 139012-96-7P 139012-97-8P
139012-98-9P 139012-99-0P 139013-00-6P 139013-01-7P 139013-02-8P
139013-03-9P 139013-04-0P 139013-05-1P 139013-06-2P 139013-07-3P
139013-08-4P 139013-09-5P 139013-10-8P 139014-45-2P
(prepn. of, as hypoglycemic and antiobesity agent)

L13 ANSWER 10 OF 23 USPATFULL
AB A process for the preparation of a compound of formula (I) ##STR1##

which is a (RR) and (RS) stereoisomer of N-(7-ethoxycarbonylmethoxy-1,2,3,4,-tetrahydronaphth-2-yl)-2-(3-chlorophenyl)-2-hydroxyethanamine and their pharmaceutically acceptable salts.

AN 94:80121 USPATFULL

TI (RR) and (RS stereoisomers of N-(7-ethoxycarbonylmethoxy-1,2,3,-tetrahydronaphth-2-yl)-2-(3-chlorophenyl)-2-hydroxyethanamine and their pharmaceutically acceptable salts

IN Boigegrain, Robert, Castelnau le Lez, France
Cecchi, Roberto, Lodi-Milan, Italy
Boveri, Sergio, Tortona, Italy

PA Sanofi, Paris, France (non-U.S. corporation)

PI US 5347037 19940913

AI US 1993-114190 19930901 (8)

RLI Continuation of Ser. No. US 1992-909315, filed on 6 Jul 1992, now abandoned which is a continuation of Ser. No. US 1991-698087, filed on 10 May 1991, now abandoned which is a division of Ser. No. US 1990-488137, filed on 5 Mar 1990, now patented, Pat. No. US 5041606 which is a division of Ser. No. US 1988-230860, filed on 11 Aug 1988, now patented, Pat. No. US 4927955

PRAI FR 1987-11498 19870812
FR 1988-7948 19880614

DT Utility

FS Granted

EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Frazier, Barbara S.

LREP Bacon & Thomas

CLMN Number of Claims: 2

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 654

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 120839-54-5P 121489-31-4P 121489-33-6P 121489-35-8P 121489-36-9P
121489-38-1P 121489-39-2P 121524-07-0P 121524-08-1P
121524-09-2P 121524-10-5P 121524-11-6P
(prepn. of, as drug)

L13 ANSWER 11 OF 23 USPATFULL

AB A process is disclosed for obtaining the R,R isomer of: ##STR1## wherein

R.sub.1 and R.sub.2 may be one or more groups which may be the same or different and are selected from the group consisting of hydrogen, C.sub.1 to C.sub.4 alkyl, C.sub.1 to C.sub.4 alkoxy, hydroxy, halogen, trifluoromethyl, carboxy, hydroxyalkyl, alkoxycarbonyl, C.sub.1 to C.sub.4 thioalkyl, sulfonyl and sulfinyl; X is a divalent radical consisting of ##STR2## wherein R' is hydrogen; R.sub.2 and R.sub.3 may be the same or different and are selected from the group consisting of hydrogen and C.sub.1 to C.sub.4 alkyl; R.sub.5 and R.sub.6 are selected from the group consisting of hydrogen, carboxy, alkoxycarbonyl, hydroxymethyl, --CH.sub.2 OCH.sub.2 COOR.sub.7 and --CH.sub.2 OCH.sub.2 CH.sub.2 OR.sub.7 where R.sub.7 is hydrogen or C.sub.1 to .sub.4 alkyl; except that R.sub.5 and R.sub.6 may not both be hydrogen; and the asterisks denote asymmetric carbon atoms; said process comprising the steps of:

(a) reacting Mosher's acid with a compound of formula I to attach a group of the formula ##STR3## at the N-9 position of a mixture of (+) and (-) enantiomers of said compound to form a new pair of diastereoisomers; and

(b) separating said new pair of diastereoisomers by HPLC and recovering the R,R isomer.

The process is based on reacting Mosher's acid with the compound of formula I and thereafter using HPLC to separate the R,R isomer.

AN 93:76671 USPATFULL
TI Substituted 5-(2-(2-aryl-2-hydroxyethyl)-amino)propyl)-1,3-benzodioxoles
IN Bloom, Jonathan D., Hartsdale, NY, United States
Claus, Thomas H., Montvale, NJ, United States
Devries, Vern G., Ridgewood, NJ, United States
Dolan, Jo A., Spring Valley, NY, United States
Dutia, Minu D., West Nyack, NY, United States
PA American Cyanamid Company, Stamford, CT, United States (U.S. corporation)
PI US 5245053 19930914
AI US 1992-896319 19920610 (7)
RLI Division of Ser. No. US 1991-742409, filed on 8 Aug 1991, now patented, Pat. No. US 5151439 which is a division of Ser. No. US 1990-519192, filed on 4 May 1990, now patented, Pat. No. US 5061727
DT Utility
FS Granted
EXNAM Primary Examiner: Daus, Donald G.
LREP Jackson, H. G., Costigan, James V.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1442
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138908-34-6P 138908-35-7P 138908-36-8P 138908-37-9P 138908-38-0P
138908-39-1P **138908-40-4P** 138908-41-5P 138908-42-6P
138908-43-7P 138908-44-8P 138908-45-9P 138908-46-0P 138908-52-8P
138908-54-0P 138908-59-5P 138908-60-8P 139012-91-2P 139012-92-3P
139012-93-4P 139012-94-5P 139012-95-6P 139012-96-7P 139012-97-8P
139012-98-9P 139012-99-0P 139013-00-6P 139013-01-7P 139013-02-8P
139013-03-9P 139013-04-0P 139013-05-1P 139013-06-2P 139013-07-3P
139013-08-4P 139013-09-5P 139013-10-8P 139014-45-2P
(prepn. of, as hypoglycemic and antiobesity agent)

L13 ANSWER 12 OF 23 USPATFULL
AB The use of a compound of the formula (I): ##STR1## wherein R is hydroxy or 2-methoxyethylamino or a pharmaceutically acceptable salt thereof, in
stimulating the `atypical` .beta.-adrenoceptors in the gastrointestinal tract and thereby inhibiting gastrointestinal motility. These compounds may be used for treating medical conditions wherein inhibition of gastrointestinal motility is thought to be of value, such as in the treatment of inflammatory bowel disease, irritable bowel syndrome (IBS),
non specific diarrhoea and dumping syndrome.
AN 93:76541 USPATFULL
TI Use of 2-(phenoxypropanolamino) ethoxphenoxy-acetic acid and its derivatives to inhibit gastrointestinal motility
IN Holloway, Brian R., Cheshire, England
Growcott, James W., Cheshire, England
PA Imperial Chemical Industries PLC, London, England (non-U.S. corporation)
PI US 5244923 19930914
AI US 1991-736952 19910730 (7)

PRAI GB 1990-16655 19900730
DT Utility
FS Granted
EXNAM Primary Examiner: Waddell, Frederick E.; Assistant Examiner: Jordan, Kimberly R.
LREP Cushman, Darby & Cushman
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 217
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 107332-57-0 115656-32-1 129689-28-7 **129689-30-1**
141269-99-0
(gastrointestinal motility inhibition with)

L13 ANSWER 13 OF 23 USPATFULL
AB 2-amino-7-hydroxytetraline ethers of formula ##STR1## wherein R' represents methyl substituted by a carboxy group or lower carbalkoxy group or a salt thereof; a process for their preparation starting from the 2-amino-7-hydroxytetraline, N-protection, O-alkylation and N-deprotection; N-protected intermediates; and use of the compounds I for the preparation of the corresponding phenylethanolaminotetralines.
AN 93:29343 USPATFULL
TI 2-amino-7-hydroxytetraline ethers
IN Boigegrain, Robert, Castelnau le Lez, France
Cecchi, Roberto, Lodi-Milano, Italy
Boveri, Sergio, Tortona, Italy
PA Sanofi, Paris, France (non-U.S. corporation)
PI US 5202466 19930413
AI US 1992-922486 19920731 (7)
RLI Division of Ser. No. US 1992-825841, filed on 28 Jan 1992, now patented,
Pat. No. US 5159103 which is a continuation of Ser. No. US 1989-365853, filed on 13 Jun 1989, now abandoned
PRAI FR 1988-7948 19880614
DT Utility
FS Granted
EXNAM Primary Examiner: Killos, Paul J.
LREP Bacon & Thomas
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 530
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 120839-54-5P 121489-31-4P 121489-33-6P 121489-35-8P 121489-36-9P
121489-38-1P 121489-39-2P 121524-07-0P 121524-08-1P
121524-09-2P 121524-10-5P 121524-11-6P
(prepn. of, as drug)

L13 ANSWER 14 OF 23 USPATFULL
AB 2-amino-7-hydroxytetraline ethers of formula ##STR1## wherein R' represents methyl substituted by a carboxy group or lower carbalkoxy group or a salt thereof; a process for their preparation starting from the 2-amino-7-hydroxytetraline, N-protection, O-alkylation and N-deprotection; N-protected intermediates; and use of the compounds I for the preparation of the corresponding phenylethanolaminotetralines.
AN 92:89212 USPATFULL
TI 2-amino-7-hydroxytetraline ethers
IN Boigegrain, Robert, Castelnau le Lez, France

Cecchi, Roberto, Lodi-Milano, Italy
Boveri, Sergio, Tortona, Italy
PA Sanofi, Paris, France (non-U.S. corporation)
PI US 5159103 19921027
AI US 1992-825841 19920128 (7)
RLI Continuation of Ser. No. US 1989-365853, filed on 13 Jun 1989, now abandoned
PRAI FR 1988-7948 19880614
DT Utility
FS Granted
EXNAM Primary Examiner: Killos, Paul J.
LREP Bacon & Thomas
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 539
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 120839-54-5P 121489-31-4P 121489-33-6P 121489-35-8P 121489-36-9P
121489-38-1P 121489-39-2P 121524-07-0P 121524-08-1P
121524-09-2P 121524-10-5P 121524-11-6P
(prepn. of, as drug)

L13 ANSWER 15 OF 23 USPATFULL
AB The present invention discloses substituted 1,3-benzodioxoles which possess anti-diabetic and/or anti-hyperglycemic and/or anti-obesity properties in humans and other animals.
AN 92:80838 USPATFULL
TI Substituted
5-(2-((2-aryl-2-hydroxyethyl)amino)propyl)-1,3-benzodioxoles
IN Bloom, Jonathan D., Hartsdale, NY, United States
Claus, Thomas H., Montvale, NJ, United States
DeVries, Vern G., Ridgewood, NJ, United States
Dolan, Jo A., Spring Valley, NY, United States
Dutia, Minu D., West Nyack, NY, United States
PA American Cyanamid Company, Stamford, CT, United States (U.S. corporation)
PI US 5151439 19920929
AI US 1991-742409 19910801 (7)
RLI Division of Ser. No. US 1990-519192, filed on 4 May 1990, now patented, Pat. No. US 5061727
DT Utility
FS Granted
EXNAM Primary Examiner: Daus, Donald G.
LREP Costigan, James V., Jackson, H. G.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1498
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138908-34-6P 138908-35-7P 138908-36-8P 138908-37-9P 138908-38-0P
138908-39-1P **138908-40-4P** 138908-41-5P 138908-42-6P
138908-43-7P 138908-44-8P 138908-45-9P 138908-46-0P 138908-52-8P
138908-54-0P 138908-59-5P 138908-60-8P 139012-91-2P 139012-92-3P
139012-93-4P 139012-94-5P 139012-95-6P 139012-96-7P 139012-97-8P
139012-98-9P 139012-99-0P 139013-00-6P 139013-01-7P 139013-02-8P
139013-03-9P 139013-04-0P 139013-05-1P 139013-06-2P 139013-07-3P
139013-08-4P 139013-09-5P 139013-10-8P 139014-45-2P
(prepn. of, as hypoglycemic and antiobesity agent)

L13 ANSWER 16 OF 23 USPATFULL
AB The present invention discloses substituted 1,3-benzodioxoles which possess anti-diabetic and/or anti-hyperglycemic and/or anti-obesity properties in humans and other animals.
AN 92:31889 USPATFULL
TI Method of increasing lean meat in edible animals
IN Bloom, Jonathan D., Hartsdale, NY, United States
Claus, Thomas H., Montvale, NJ, United States
DeVries, Vern G., Ridgewood, NJ, United States
Dolan, Jo A., Spring Valley, NY, United States
Dutia, Minu D., West Nyack, NY, United States
PA American Cyanamid Company, Stamford, CT, United States (U.S. corporation)
PI US 5106867 19920421
AI US 1991-679313 19910405 (7)
RLI Continuation-in-part of Ser. No. US 1990-519192, filed on 4 May 1990
DT Utility
FS Granted
EXNAM Primary Examiner: Daus, Donald G.
LREP Jackson, H. G.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1469
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138908-34-6P 138908-35-7P 138908-36-8P **138908-40-4P**
138908-41-5P 138908-54-0P 138908-59-5P 138908-60-8P 139014-45-2P
143485-19-2P
(prepn. of, as antiobesity agent, antidiabetic, and animal food additive)

L13 ANSWER 17 OF 23 USPATFULL
AB The present invention discloses substituted 1,3-benzodioxoles which possess anti-diabetic and/or anti-hyperglycemic and/or anti-obesity properties in humans and other animals.
AN 91:89072 USPATFULL
TI Substituted
5-(2-((2-aryl-2-hydroxyethyl)amino)propyl)-1,3-benzodioxoles
IN Bloom, Jonathan D., Hartsdale, NY, United States
Claus, Thomas H., Montvale, NJ, United States
DeVries, Vern G., Ridgewood, NJ, United States
Dolan, Jo A., Spring Valley, NY, United States
Dutia, Minu D., West Nyack, NY, United States
PA American Cyanamid Company, Stamford, CT, United States (U.S. corporation)
PI US 5061727 19911029
AI US 1990-519192 19900504 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Daus, Donald G.
LREP Jackson, H. G.
CLMN Number of Claims: 58
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1608
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138908-34-6P 138908-35-7P 138908-36-8P 138908-37-9P 138908-38-0P
138908-39-1P **138908-40-4P** 138908-41-5P 138908-42-6P
138908-43-7P 138908-44-8P 138908-45-9P 138908-46-0P 138908-52-8P

138908-54-0P 138908-59-5P 138908-60-8P 139012-91-2P 139012-92-3P
139012-93-4P 139012-94-5P 139012-95-6P 139012-96-7P 139012-97-8P
139012-98-9P 139012-99-0P 139013-00-6P 139013-01-7P 139013-02-8P
139013-03-9P 139013-04-0P 139013-05-1P 139013-06-2P 139013-07-3P
139013-08-4P 139013-09-5P 139013-10-8P 139014-45-2P
(prepn. of, as hypoglycemic and antiobesity agent)

L13 ANSWER 18 OF 23 USPATFULL
AB A process for the preparation of a compound of formula ##STR1## wherein X represents hydrogen, halogen, trifluoromethyl or lower alkyl group; W represents methyl, Q represents hydrogen or W and Q, together, form an ethylene group and R' represents a lower alkyl group which comprises protecting the amino group of the phenol corresponding to the compound of formula I, submitting the compound thus obtained to an alkylation (with a compound of formula Hal--CH.sub.2 --COOR', wherein R' is as defined hereinabove for the formula I and Hal is chlorine, bromine or iodine) and then releasing the amino group of the product thus obtained.
AN 91:66959 USPATFULL
TI Process for the O-alkylation of N-(hydroxy)aralkylphenylethanolamines
IN Boigegrain, Robert, Castelnau le Lez, France
Cecchi, Roberto, Lodi-Milan, Italy
Boveri, Sergio, Tortona, Italy
PA Sanofi, United States (non-U.S. corporation)
PI US 5041606 19910820
AI US 1990-488137 19900305 (7)
RLI Division of Ser. No. US 1988-230860, filed on 11 Aug 1988, now patented,
Pat. No. US 4927955
PRAI FR 1987-11498 19870812
FR 1988-7948 19880614
DT Utility
FS Granted
EXNAM Primary Examiner: Gray, Bruce
LREP Bacon & Thomas
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 120839-54-5P 121489-31-4P 121489-33-6P 121489-35-8P 121489-36-9P
121489-38-1P 121489-39-2P 121524-07-0P 121524-08-1P
121524-09-2P 121524-10-5P 121524-11-6P
(prepn. of, as drug)

L13 ANSWER 19 OF 23 USPATFULL
AB A process for the preparation of a compound of formula ##STR1## wherein X represents hydrogen, halogen, trifluoromethyl or lower alkyl group; W represents methyl, Q represents hydrogen or W and Q, together, form an ethylene group and R' represents a lower alkyl group which comprises protecting the amino group of the phenol corresponding to the compound of formula I, submitting the compound thus obtained to an alkylation (with a compound of formula Hal--CH.sub.2 --COOR', wherein R' is as defined hereinabove for the formula I and Hal is chlorine, bromine or iodine) and then releasing the amino group of the product thus obtained.
AN 90:40689 USPATFULL
TI Process for the O-alkylation of N-(hydroxy)aralkylphenylethanolamines
IN Boigegrain, Robert, Castelnau Le Lez, France

Cecchi, Roberto, Lodi-Milan, Italy
Boveri, Sergio, Tortona, Italy
PA Sanofi, Paris, France (non-U.S. corporation)
PI US 4927955 19900522
AI US 1988-230860 19880811 (7)
PRAI FR 1987-11498 19870812
FR 1988-7948 19880614
DT Utility
FS Granted
EXNAM Primary Examiner: Gray, Bruce
LREP Bacon & Thomas
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 120839-54-5P 121489-31-4P 121489-33-6P 121489-35-8P 121489-36-9P
121489-38-1P 121489-39-2P 121524-07-0P 121524-08-1P
121524-09-2P 121524-10-5P 121524-11-6P
(prepn. of, as drug)

L13 ANSWER 20 OF 23 USPATFULL
AB The invention concerns novel phenoxyacetic acid amide derivatives of the
formula I (and pharmaceutically acceptable salts thereof) in which R.sup.1 is hydrogen or fluoro, R.sup.2 is phenyl, cycloalkyl, alkyl or alkenyl as defined herein, and R.sup.3 is hydrogen, methyl or ethyl, or R.sup.2 and R.sup.3 together form polymethylene as defined herein. The invention also includes pharmaceutical compositions containing the amide
derivatives, means for the manufacture of the said derivatives and for their use in the treatment of obesity and related conditions and/or in the manufacture of novel medicaments.
AN 90:40570 USPATFULL
TI Amide derivatives
IN Holloway, Brian R., Congleton, England
Howe, Ralph, MacClesfield, England
Rao, Balbir S., Holmes Chapel, England
Stribling, Donald, Prestbury, England
PA Imperial Chemical Industries PLC, London, England (non-U.S. corporation)
PI US 4927836 19900522
AI US 1988-213259 19880629 (7)
RLI Continuation-in-part of Ser. No. US 1987-75983, filed on 21 Jul 1987, now abandoned
PRAI GB 1986-17986 19860723
GB 1987-1832 19870128
DT Utility
FS Granted
EXNAM Primary Examiner: Hollrah, Glennon H.; Assistant Examiner: Treanor, Susan P.
LREP Cushman, Darby & Cushman
CLMN Number of Claims: 14
ECL Exemplary Claim: 1,14
DRWN No Drawings
LN.CNT 822
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 587-65-5P, N-Phenyl-2-chloroacetamide 13916-39-7P 107332-58-1P
107332-59-2P 107332-60-5P 107332-61-6P 107332-62-7P 107332-63-8P

107332-64-9P 107332-65-0P 107332-66-1P 107332-69-4P 107332-79-6P
107332-81-0P 107332-82-1P 107332-83-2P, 3-(2-Bromoethoxy)phenol
107332-84-3P 107332-93-4P 108856-98-0P 129689-29-8P
129689-30-1P
(prepn. and reaction of, in prepn. of antiobesity agent)

L13 ANSWER 21 OF 23 USPATFULL
AB Compounds of formula (I): ##STR1## or a pharmaceutically acceptable salt
thereof,

in which

R.sup.1 is hydrogen, halogen, or trifluoromethyl,

R.sup.2 is hydrogen or halogen,

R.sup.3 is hydroxyl, C.sub.1-6 alkoxy or ##STR2## where R.sup.8 and R.sup.9 are each hydrogen or C.sub.1-6 alkyl; R.sup.4 is hydrogen or C.sub.1-6 alkyl; R.sup.5 is hydrogen, C.sub.1-6 alkyl, C.sub.1-6 alkyl optionally substituted by hydroxy; cyano, C.sub.1-6 alkenyl or C.sub.1-6
alkynyl optionally substituted by carboxy or esters and amides thereof, phenyl, C.sub.1-6 alkyl phenyl or a group ##STR3## wherein R.sup.12 and
R.sup.13 are each hydrogen or C.sub.1-6 alkyl or together, along with the nitrogen to which they are attached, form a 5- or 6-membered ring and m is 1 or 2;

R.sup.6 is hydrogen or methyl:

R.sup.7 is --O(CH.sub.2).sub.a CO.sub.2 H, --O(CH.sub.2).sub.b M, --CO.sub.2 H; or amide thereof in which

a is an integer from 1 to 6,

b is an integer from 2 to 7, and

M is hydroxy, C.sub.1-6 alkoxy or ##STR4## in which R.sup.10 and R.sup.11 are each hydrogen or C.sub.1-6 alkyl or ##STR5## together form
a five or six membered ring; and n is 1 or 2; with the proviso that when
n is 2 and R.sup.1, R.sup.2, R.sup.4 and R.sup.6 are each hydrogen and R.sup.3 is hydroxyl, R.sup.5 is not hydroxymethyl or 1-hydroxy ethyl when R.sup.7 is CONH.sub.2 ; processes for preparing such compounds and their use in medicine.
AN 89:9399 USPATFULL
TI Tertiary amines
IN Berge, John, Redhill, England
Hindley, Richard M., Reigate, England
PA Beecham Group plc, Middlesex, England (non-U.S. corporation)
PI US 4803293 19890207
AI US 1987-17002 19870218 (7)
RLI Continuation of Ser. No. US 1984-667757, filed on 2 Nov 1984, now abandoned
PRAI GB 1983-29490 19831104
GB 1983-34294 19831222
DT Utility

FS Granted
EXNAM Primary Examiner: Shippen, Michael L.; Assistant Examiner: Gray, Bruce D.
LREP Hopgood, Calimafde, Kalil, Blaustein & Judlowe
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 613
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 77955-40-9 83195-54-4 86615-41-0 **86615-96-5** 87857-42-9
96798-24-2 96798-25-3 99386-62-6
(N-alkylation of)

L13 ANSWER 22 OF 23 USPATFULL
AB A compound of formula (I) ##STR1## or a pharmaceutically acceptable salt
thereof, in which R.sup.1 is hydrogen, halogen, or trifluoromethyl;

R.sup.2 is hydrogen or halogen;

R.sup.3 is hydrogen or methyl;

R.sup.4 is --O(CH.sub.2).sub.a CO.sub.2 H or an ester or amide derivative thereof, O(CH.sub.2).sub.b M or --CO.sub.2 H or an ester or amide derivative thereof

wherein

a is an integer from 1 to 6,

b is an integer from 2 to 7, and

M is hydroxy, C.sub.1-6 alkoxy or ##STR2## wherein R.sup.6 and R.sup.7 are each hydrogen or C.sub.1-6 alkyl or ##STR3## together form a five or six membered ring; R.sup.5 is C.sub.1-6 alkyl; C.sub.1-6 alkyl substituted by carboxy or esters and amides thereof; or phenyl optionally substituted by C.sub.1-6 alkyl, halogen, alkoxy or trifluoromethyl;

R.sup.8 is hydrogen or C.sub.1-6 alkyl or R.sup.8 together with

R.sup.5 form a carbocyclic ring; and

n is 1 or 2.

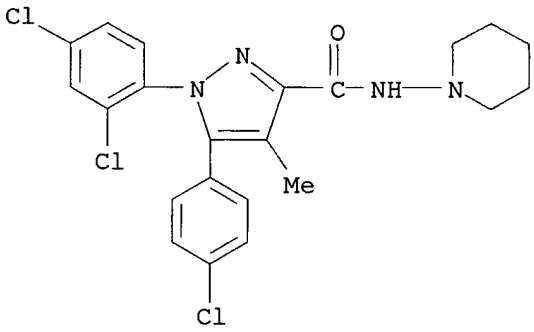
Processes for preparing these compounds and their use in therapy is also
described.
AN 86:36899 USPATFULL
TI Hydroxymorpholine derivatives
IN Ainsworth, Anthony T., Bishop's Stortford, England
Hindley, Richard M., Reigate, England
PA Beecham Group p.l.c., England (non-U.S. corporation)
PI US 4596800 19860624
AI US 1985-756795 19850719 (6)
PRAI GB 1984-18657 19840721
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.

LREP Hopgood, Calimafde, Kalil, Blaustein & Judlowe
CLMN Number of Claims: 7
ECL Exemplary Claim: 1,6
DRWN No Drawings
LN.CNT 478
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 70-11-1 78-95-5 638-07-3 814-75-5 822-87-7 83195-54-4
86615-96-5 103338-04-1 103420-66-2
(reaction of, in hydroxymorpholine deriv. prepn.)

L13 ANSWER 23 OF 23 USPATFULL
AB The compounds of formula (II): ##STR1## in which R.sub.1 is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group; R.sub.2 is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group; R.sub.3 is a hydrogen, chlorine or bromine atom or a hydroxyl group, R.sub.4 is a hydrogen atom or a methyl group; R.sub.5 is a hydrogen atom or a methyl group; R.sub.6 is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group; X is an oxygen atom or a bond; Y is an alkylene group of up to 6 carbon atoms or a bond; and Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms, have been found to possess anti-obesity and/or anti-hyperglycaemic activity.
AN 82:32762 USPATFULL
TI Ethanamine derivatives their preparation and use in pharmaceutical compositions
IN Ainsworth, Anthony T., Cranleigh, England
Smith, David G., Redhill, England
PA Beecham Group Limited, England (non-U.S. corporation)
PI US 4338333 19820706
AI US 1980-157555 19800609 (6)
PRAI GB 1979-21038 19790616
DT Utility
FS Granted
EXNAM Primary Examiner: Breitenstein, G. T.
LREP Jacobs & Jacobs
CLMN Number of Claims: 16
ECL Exemplary Claim: 1,13,16
DRWN No Drawings
LN.CNT 903
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 78069-20-2P 78069-21-3P **78069-22-4P** 78069-23-5P
78069-29-1P 78069-30-4P 78069-31-5P 78069-32-6P 78069-33-7P
78069-34-8P 78069-35-9P 78069-36-0P
(prepn. and pharmacol. activity of)

=>

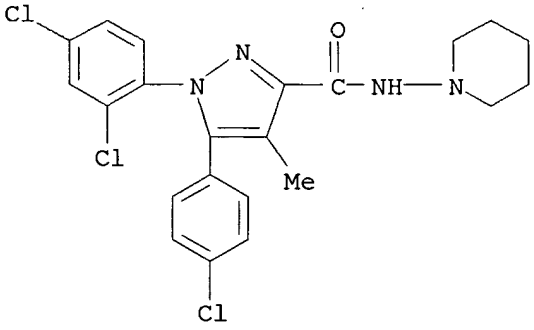
L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 158681-13-1 REGISTRY
CN 1H-Pyrazole-3-carboxamide, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-N-1-piperidinyl-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **SR 141716A**
MF C22 H21 Cl3 N4 O . Cl H
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CEN, EMBASE, MEDLINE, PHAR, PROMT, TOXCENTER, USPATFULL
CRN (168273-06-1)



● HCl

170 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
170 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 168273-06-1 REGISTRY
CN 1H-Pyrazole-3-carboxamide, 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-N-1-piperidinyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Rimonabant
CN **SR 141716**
FS 3D CONCORD
MF C22 H21 Cl3 N4 O
CI COM
SR CA
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, CASREACT, CIN, DRUGNL, DRUGPAT, DRUGUPDATES, PROMT, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

58 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
58 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L4 ANSWER 1 OF 4 USPATFULL
AN 2001:191121 USPATFULL
TI Therapeutic use of compounds with .beta.3-agonist activity
IN Advenier, Charles, Paris, France
Manara, Luciano, Pietra Morazzi, Italy
PA Sanofi-Synthelabo, Paris, France (non-U.S. corporation)
PI US 6310050 B1 20011030
WO 2000021508 20000420
AI US 2001-807342 20010524 (9)
WO 1999-FR2308 19990929
20010524 PCT 371 date
20010524 PCT 102(e) date
PRAI FR 1998-12877 19981014
DT Utility
FS GRANTED
EXNAM Primary Examiner: Henley, III, Raymond
LREP Alexander, Michael D.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 238
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the method of use of compounds with B.sub.3 -agonist activity for inhibiting uterine contractions, preventing or slowing down premature labor, or for the treatment and/or prophylaxis of dysmenorrhea.
IT 159182-43-1 159183-92-3 166740-74-5 170685-57-1 172902-05-5
173900-99-7 179819-89-7 188407-40-1 210757-90-7 **210757-91-8**
264134-39-6 264134-40-9 264134-41-0 264134-42-1 264134-43-2
(use of beta-3-agonist compds. for inhibition of uterine contractions)

L4 ANSWER 2 OF 4 USPATFULL
AN 2001:75445 USPATFULL
TI Use of agonists of adrenergic .beta.-3 receptors for preparing wound-healing medicines
IN Bernat, Andre, Cugnaux, France
Herbert, Jean-Marc, Tournefeuille, France
Arnone, Michele, Ramonville St Agne, France
PA Sanofi-Synthelabo, Paris, France (non-U.S. corporation)
PI US 6235793 B1 20010522
WO 9831357 19980723
AI US 1999-341656 19990715 (9)
WO 1998-FR105 19980121
19990715 PCT 371 date
19990715 PCT 102(e) date
PRAI FR 1997-584 19970121
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.; Assistant Examiner: Kim, Vickie
LREP Alexander, Michael D., Dupont, Paul E.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 462
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the use of .beta..sub.3 -adrenergic receptor agonists for the preparation of healing drugs and to the pharmaceutical compositions for said use.
IT 210757-90-7 **210757-91-8**
(use of agonists of beta-3 adrenergic receptors for prepg. wound-healing medicines)

L4 ANSWER 3 OF 4 USPATFULL

AN 93:20546 USPATFULL
TI Anti-hypertensive sulfonanilides
IN McDermed, John D., Chapel Hill, NC, United States
Tadepalli, Anjaneyulu S., Durham, NC, United States
Chang, Vincent H., Freeport, Bahamas
Hurley, Kevin P., Durham, NC, United States
Freeman, Harold S., Raleigh, NC, United States
PA Burroughs Wellcome Co., Research Triangle Park, NC, United States (U.S. corporation)
PI US 5194450 19930316
AI US 1991-783689 19911028 (7)
RLI Continuation of Ser. No. US 1990-577057, filed on 31 Aug 1990, now abandoned which is a continuation of Ser. No. US 1990-479181, filed on 12 Feb 1990, now abandoned which is a continuation of Ser. No. US 1989-340437, filed on 19 Apr 1989, now abandoned
PRAI GB 1988-9314 19880420
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: O'Sullivan, P.
LREP Brown, Donald, Nielsen, Lawrence A., Green, Hannah O.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 971
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is concerned with compounds of formula (I) ##STR1## wherein R.sup.1 is hydrogen or C.sub.1-4 alkoxy;

R.sub.2 is carbonyl, hydroxymethylene, or methylene; and

R.sub.3 is hydrogen or hydroxy;

and salts thereof, provided that when R.sub.1 is hydrogen and R.sub.2 is carbonyl, R.sub.3 is not hydroxy, with processes for preparing same and with their use in medicine for the treatment of hypertension.
IT 129280-07-5P 129280-08-6P 129280-09-7P 129280-10-0P 129280-11-1P
129280-12-2P 129280-13-3P 129280-14-4P 129280-19-9P
129280-22-4P 129280-27-9P 129314-28-9P 129314-29-0P 129314-30-3P
129314-31-4P 129314-32-5P 129314-33-6P 129314-34-7P 129314-35-8P
129314-36-9P
(prepn. of, as antihypertensive)

L4 ANSWER 4 OF 4 USPATFULL
AN 92:27559 USPATFULL
TI Antihypertensive sulfonanilides
IN McDermed, John D., Chapel Hill, NC, United States
Tadepalli, Anjaneyulu S., Durham, NC, United States
Chang, Vincent H., Freeport, Bahamas
Hurley, Kevin P., Durham, NC, United States
PA Burroughs Wellcome Co., Research Triangle Park, NC, United States (U.S. corporation)
PI US 5102914 19920407
AI US 1989-455909 19891218 (7)
RLI Continuation of Ser. No. US 1989-340226, filed on 19 Apr 1989, now abandoned
PRAI GB 1988-9314 19880420
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Bembenick, B.
LREP Brown, Donald, Green, Hannah O., Nielsen, Lawrence A.
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 1014
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is concerned with compounds of formula (I) ##STR1## wherein R.sub.1 is hydrogen;

R.sub.2 is carbonyl; and

R.sub.3 is hydroxy;

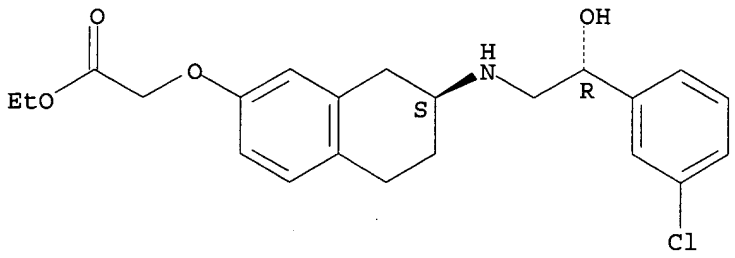
and salts thereof, with processes for preparing same and with their use in medicine for the treatment of hypertension.

IT 129280-07-5P 129280-08-6P 129280-09-7P 129280-10-0P 129280-11-1P
129280-12-2P 129280-13-3P 129280-14-4P 129280-19-9P
129280-22-4P 129280-27-9P 129314-28-9P 129314-29-0P 129314-30-3P
129314-31-4P 129314-32-5P 129314-33-6P 129314-34-7P 129314-35-8P
129314-36-9P
(prepn. of, as antihypertensive)

=>

L2 ANSWER 1 OF 3 USPATFULL
AN 2002:332735 USPATFULL
TI Propanolamine derivatives
IN Taniguchi, Kiyoshi, Kobe, JAPAN
Sakurai, Minoru, Toyonaka, JAPAN
Fujii, Naoaki, Takatsuki, JAPAN
Hosoi, Kumi, Susono, JAPAN
Tomishima, Yasuyo, Osaka, JAPAN
Takasugi, Hisashi, Sakai, JAPAN
Sogabe, Hajime, Tokyo, JAPAN
Ishikawa, Hirofumi, Suita, JAPAN
Hanioka, Naomi, Minoo, JAPAN
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, JAPAN (non-U.S. corporation)
PI US 6495546 B1 20021217
WO 9951564 19991014
AI US 2000-646878 20001122 (9)
WO 1999-JP1500 19990325
20001122 PCT 371 date
PRAI AU 1998-2826 19980406
AU 1998-5058 19980804
DT Utility
FS GRANTED
EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Covington, Raymond
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 4667
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . urinary stress incontinence or the like; and for the treatment and/or prevention of pancreatitis, obesity, diabetes, glycosuria, hyperlipidemia, hypertension, atherosclerosis, **glaucoma**, melancholia, depression and the like.
SUMM . . . incontinence, urinary incontinence, or the like; and for the treatment and/or prevention of pancreatitis, obesity, diabetes, glycosuria, hyperlipidemia, hypertension, atherosclerosis, **glaucoma**, melancholia, depression, and the like.
IT 116049-79-7 **121524-09-2** 173901-95-6 193759-91-0
246262-41-9
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)
IT **121524-09-2**
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)
RN 121524-09-2 USPATFULL
CN Acetic acid, [[(7S)-7-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

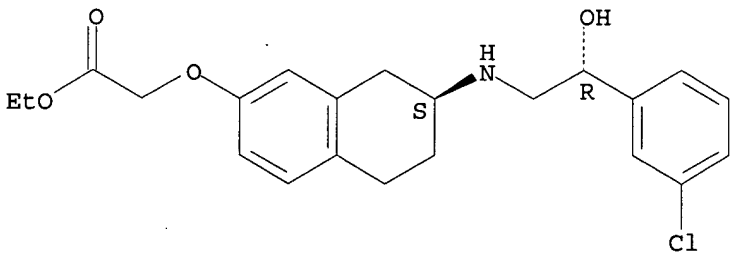


● HCl

L2 ANSWER 2 OF 3 USPATFULL
AN 2002:222002 USPATFULL
TI Propanolamine derivatives
IN Taniguchi, Kiyoshi, Hyogo, JAPAN
Sakurai, Minoru, Osaka, JAPAN
Fujii, Naoaki, Osaka, JAPAN
Hosoi, Kumi, Shizuoka, JAPAN
Tomishima, Yasuyo, Osaka, JAPAN
Takasugi, Hisashi, Osaka, JAPAN
Sogabe, Hajime, Tokyo, JAPAN
Ishikawa, Hirofumi, Osaka, JAPAN
Hanioka, Naomi, Osaka, JAPAN
PA Fujisawa Pharmaceutical Co. Ltd., Osaka-shi, JAPAN (non-U.S. corporation)
PI US 2002120148 A1 20020829
AI US 2002-74020 A1 20020214 (10)
RLI Continuation of Ser. No. US 2000-646878, filed on 22 Nov 2000, PENDING
PRAI WO 1999-JP1500 19990325
AU 1998-2826 19980406
AU 1998-5058 19980804
DT Utility
FS APPLICATION
LREP OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . urinary stress incontinence or the like; and for the treatment and/or prevention of pancreatitis, obesity, diabetes, glycosuria, hyperlipidemia, hypertension, atherosclerosis, **glaucoma**, melancholia, depression and the like.
SUMM . . . incontinence, urinary incontinence, or the like; and for the treatment and/or prevention of pancreatitis, obesity, diabetes, glycosuria, hyperlipidemia, hypertension, atherosclerosis, **glaucoma**, melancholia, depression, and the like.
IT 116049-79-7 **121524-09-2** 173901-95-6 193759-91-0 246262-41-9
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)
IT **121524-09-2**
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)
RN 121524-09-2 USPATFULL
CN Acetic acid, [[(7S)-7-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-

5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester, hydrochloride (9CI) (CA INDEX NAME)

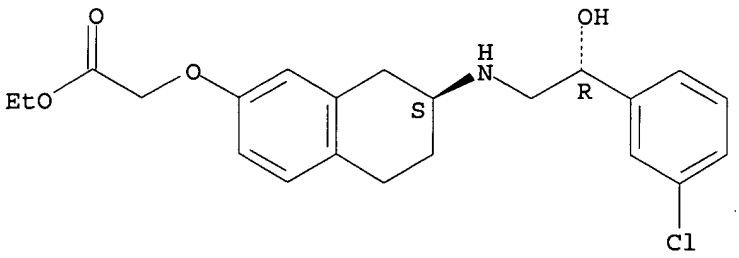
Absolute stereochemistry.



● HCl

L2 ANSWER 3 OF 3 USPATFULL
AN 96:9522 USPATFULL
TI {(7S)-7-[(2R)-2-(3-chlorophenyl)-2-hydroxyethylamino)-2-hydroxyethylamino]5,} acetic acid and its pharmaceutically acceptable salts
IN Baroni, Marco, Vanzago, Italy
Cecchi, Roberto, Lodi, Italy
Croci, Tiziano, Milan, Italy
PA Sanofi, Paris, France (non-U.S. corporation)
PI US 5488151 19960130
AI US 1994-250830 19940531 (8)
PRAI EP 1993-401375 19930528
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Frazier, Barbara S.
LREP Bacon & Thomas
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 220
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . in the treatment of eye complaints, especially for the control of intraocular pressure and the treatment of ocular hypertension and **glaucoma**.
IT **121524-08-1**
(prepn. of .beta.3-adrenergic receptor agonist by hydrolysis of)
IT **121524-08-1**
(prepn. of .beta.3-adrenergic receptor agonist by hydrolysis of)
RN 121524-08-1 USPATFULL
CN Acetic acid, [[(2S)-7-[[(2R)-2-(3-chlorophenyl)-2-hydroxyethyl]amino]-5,6,7,8-tetrahydro-2-naphthalenyl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.


O
EtO
O
H
N
S
OH
R
Cl

=>

L3 ANSWER 1 OF 5 USPATFULL
AN 2002:332735 USPATFULL
TI Propanolamine derivatives
IN Taniguchi, Kiyoshi, Kobe, JAPAN
Sakurai, Minoru, Toyonaka, JAPAN
Fujii, Naoaki, Takatsuki, JAPAN
Hosoi, Kumi, Susono, JAPAN
Tomishima, Yasuyo, Osaka, JAPAN
Takasugi, Hisashi, Sakai, JAPAN
Sogabe, Hajime, Tokyo, JAPAN
Ishikawa, Hirofumi, Suita, JAPAN
Hanioka, Naomi, Minoo, JAPAN
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, JAPAN (non-U.S. corporation)
PI US 6495546 B1 20021217
WO 9951564 19991014
AI US 2000-646878 20001122 (9)
WO 1999-JP1500 19990325
20001122 PCT 371 date
PRAI AU 1998-2826 19980406
AU 1998-5058 19980804
DT Utility
FS GRANTED
EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Covington, Raymond
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 4667
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . neurogenic bladder dysfunction, nocturia, unstable bladder, cystospasm, chronic cystitis, chronic prostatitis, overflow incontinence, passive incontinence, reflux incontinence, urge incontinence, urinary **stress** incontinence or the like; and for the treatment and/or prevention of pancreatitis, obesity, diabetes, glycosuria, hyperlipidemia, hypertension, atherosclerosis, glaucoma, melancholia,. . .
IT 116049-79-7 **121524-09-2** 173901-95-6 193759-91-0
246262-41-9
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

L3 ANSWER 2 OF 5 USPATFULL
AN 2002:222002 USPATFULL
TI Propanolamine derivatives
IN Taniguchi, Kiyoshi, Hyogo, JAPAN
Sakurai, Minoru, Osaka, JAPAN
Fujii, Naoaki, Osaka, JAPAN
Hosoi, Kumi, Shizuoka, JAPAN
Tomishima, Yasuyo, Osaka, JAPAN
Takasugi, Hisashi, Osaka, JAPAN
Sogabe, Hajime, Tokyo, JAPAN
Ishikawa, Hirofumi, Osaka, JAPAN
Hanioka, Naomi, Osaka, JAPAN
PA Fujisawa Pharmaceutical Co. Ltd., Osaka-shi, JAPAN (non-U.S. corporation)
PI US 2002120148 A1 20020829
AI US 2002-74020 A1 20020214 (10)
RLI Continuation of Ser. No. US 2000-646878, filed on 22 Nov 2000, PENDING
PRAI WO 1999-JP1500 19990325
AU 1998-2826 19980406
AU 1998-5058 19980804

DT Utility
FS APPLICATION
LREP OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755 JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . neurogenic bladder dysfunction, nocturia, unstable bladder, cystospasm, chronic cystitis, chronic prostatitis, overflow incontinence, passive incontinence, reflux incontinence, urge incontinence, urinary **stress** incontinence or the like; and for the treatment and/or prevention of pancreatitis, obesity, diabetes, glycosuria, hyperlipidemia, hypertension, atherosclerosis, glaucoma, melancholia,. . .
IT 116049-79-7 **121524-09-2** 173901-95-6 193759-91-0 246262-41-9
(comparison compd.; prepn. of propanolamine tetrahydro-5H-benzocycloheptene derivs. as .beta.3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

L3 ANSWER 3 OF 5 USPATFULL
AN 2001:165828 USPATFULL
TI Method of reducing craving in mammals
IN Coffin, Vicki L., Basking Ridge, NJ, United States
Glue, Paul W., Flemington, NJ, United States
PI US 2001025038 A1 20010927
AI US 2001-846170 A1 20010501 (9)
RLI Division of Ser. No. US 1998-178447, filed on 23 Oct 1998, PENDING
PRAI US 1997-64563P 19971028 (60)
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 594
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD [0030] FIGS. 7 and 8 represent plots of the subjective euphoria and **anxiety**, respectively, before and after cocaine administration with varying dosages of a preferred D.sub.1/D.sub.5 antagonist and with a placebo.
DETD . . . been pre-treated with SCH 39166, particularly a dose of 100 mg. FIG. 8 shows that the dysphoric effects, such as **anxiety**, after cocaine administration were lower in those patients who had been pre-treated with SCH 39166. As may be seen in. . .
IT 34911-55-2, Bupropion 36505-84-7, Buspirone 58939-37-0, A 69024 67287-49-4, SKF 38393 87134-87-0, Sch 23390 maleate **121524-09-2**, SR 58611a 150490-85-0, NNC-22-0010 171285-42-0, JHS 136 171285-53-3, JHS 271 175413-88-4, JHS 198 190133-94-9, SCH 39166 193480-75-0 224031-15-6, BTS-73-947
(method of reducing nicotine and tobacco craving in mammals)

L3 ANSWER 4 OF 5 USPATFULL
AN 2001:112314 USPATFULL
TI Method of reducing nicotine and tobacco craving in mammals
IN Coffin, Vicki L., Basking Ridge, NJ, United States
Glue, Paul W., Flemington, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 6262049 B1 20010717
AI US 1998-178447 19981023 (9)
PRAI US 1997-64563P 19971028 (60)

DT Utility
FS GRANTED
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Mazer, Edward H.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 570
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD FIGS. 7 and 8 represent plots of the subjective euphoria and **anxiety**, respectively, before and after cocaine administration with varying dosages of a preferred D.sub.1 /D.sub.5 antagonist and with a placebo.
DETD . . . been pre-treated with SCH 39166, particularly a dose of 100 mg. FIG. 8 shows that the dysphoric effects, such as **anxiety**, after cocaine administration were lower in those patients who had been pre-treated with SCH 39166. As may be seen in. . .
IT 34911-55-2, Bupropion 36505-84-7, Buspirone 58939-37-0, A 69024 67287-49-4, SKF 38393 87134-87-0, Sch 23390 maleate **121524-09-2**, SR 58611a 150490-85-0, NNC-22-0010 171285-42-0, JHS 136 171285-53-3, JHS 271 175413-88-4, JHS 198 190133-94-9, SCH 39166 193480-75-0 224031-15-6, BTS-73-947
(method of reducing nicotine and tobacco craving in mammals)

L3 ANSWER 5 OF 5 USPATFULL
AN 96:9522 USPATFULL
TI {(7S)-7-[(2R)-2-(3-chlorophenyl)-2-hydroxyethylamino)-2-hydroxyethylamino]5,} acetic acid and its pharmaceutically acceptable salts
IN Baroni, Marco, Vanzago, Italy
Cecchi, Roberto, Lodi, Italy
Croci, Tiziano, Milan, Italy
PA Sanofi, Paris, France (non-U.S. corporation)
PI US 5488151 19960130
AI US 1994-250830 19940531 (8)
PRAI EP 1993-401375 19930528
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Frazier, Barbara S.
LREP Bacon & Thomas
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 220
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . acceptable salts can also be used for the preparation of drugs for combating depression, anxiodepressive disorders and certain consequences of **stress**, such as **anxiety**.
DETD . . . acid of formula (I) and its pharmaceutically acceptable salts can also be used in depressive and anxio-depressive states and in **anxiety** caused by **stress**.
CLM What is claimed:
10. The method of claim 6 for the treatment of depressive and anxio-depressive states and **anxiety** caused by **stress**
.

IT **121524-08-1**
(prepn. of .beta.3-adrenergic receptor agonist by hydrolysis of)

=>

(FILE 'HOME' ENTERED AT 11:29:07 ON 09 JUN 2003)

FILE 'USPATFULL' ENTERED AT 11:29:21 ON 09 JUN 2003

L1 11 S 121524-09-2/RN OR 121524-08-1/RN

L2 3 S L1 AND GLAUCOMA

L3 5 S L1 AND (IMMUNOMODULATION OR MIGRAINE OR ASTHMA OR EPILEPSY OR

L1 ANSWER 1 OF 1 INPADOC COPYRIGHT 2003 EPO

PATENT FAMILY INFORMATION
AN 9258163 INPADOC

PRAI			AI		
CA 1990-2033243	A3	19901227	CA 1990-2222657	A	19901227
EP 1990-403342	A	19901126	AT 1990-403762	EP	19901226
			CA 1990-2033243	A	19901227
			CA 1990-2222657	A	19901227
			DE 1990-403762	EP	19901226
			DE 1990-69007603	A	19901226
			DK 1990-403762	A	19901226
			EP 1990-403762	A	19901226
			ES 1990-403762	EP	19901226
			IE 1990-4662	A	19901221
			JP 1990-418873	A	19901227
			PT 1990-96391	A	19901228
			US 1990-301050	A	19901228
EP 1990-403762	A	19901226	AT 1990-403762	EP	19901226
FR 1989-17465	A	19891229	AT 1990-403762	EP	19901226
			CA 1990-2033243	A	19901227
			CA 1990-2222657	A	19901227
			DE 1990-403762	EP	19901226
			DE 1990-69007603	A	19901226
			DK 1990-403762	A	19901226
			EP 1990-403762	A	19901226
			ES 1990-403762	EP	19901226
			FR 1989-17465	A	19891229
			IE 1990-4662	A	19901221
			JP 1990-418873	A	19901227
			PT 1990-96391	A	19901228
			US 1990-301050	A	19901228

AI			PI		
AT 1990-403762	EP	19901226	AT 103269	E	19940415
CA 1990-2033243	A	19901227	CA 2033243	AA	19910630
			CA 2033243	C	19980707
CA 1990-2222657	A	19901227	CA 2222657	C	20011023
DE 1990-403762	EP	19901226	DE 69007603	C0	19940428
DE 1990-69007603	A	19901226	DE 69007603	T2	19940630
DK 1990-403762	A	19901226	DK 436435	T3	19940725
EP 1990-403762	A	19901226	EP 436435	A1	19910710
			EP 436435	B1	19940323
ES 1990-403762	EP	19901226	ES 2054304	T3	19940801
FR 1989-17465	A	19891229	FR 2656607	A1	19910705
			FR 2656607	B1	19940311
IE 1990-4662	A	19901221	IE 65511	B	19951101
			IE 9004662	A1	19910717
JP 1990-418873	A	19901227	JP 04210663	A2	19920731
			JP 2521191B	B2	19960731
PT 1990-96391	A	19901228	PT 96391	A	19911015
			PT 96391	B	19980630
US 1990-301050	A	19901228	US 5130339	A	19920714

4 priorities, 13 applications, 19 publications

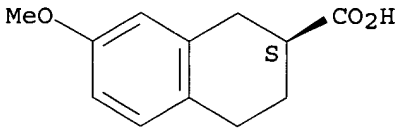
=>

EP0436435

L11 ANSWER 1 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136844-70-7** REGISTRY

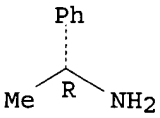
CM 1

Absolute stereochemistry.



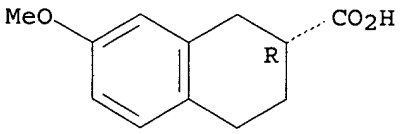
CM 2

Absolute stereochemistry.



L11 ANSWER 2 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136781-73-2** REGISTRY

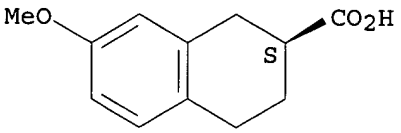
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

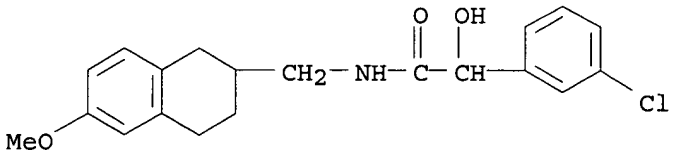
L11 ANSWER 3 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136781-72-1** REGISTRY

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

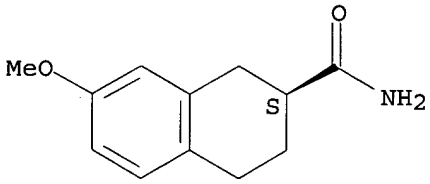
L11 ANSWER 4 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136770-49-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 5 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136770-48-4** REGISTRY

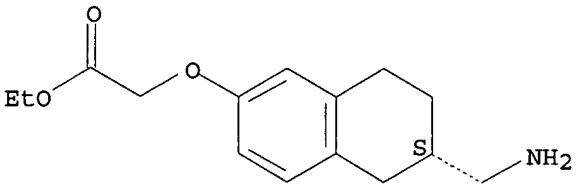
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 6 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-74-5** REGISTRY

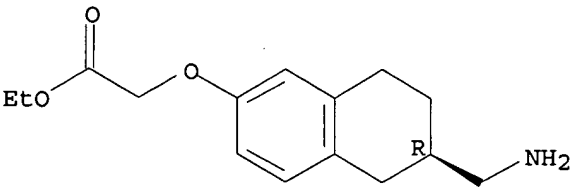
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 7 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-73-4** REGISTRY

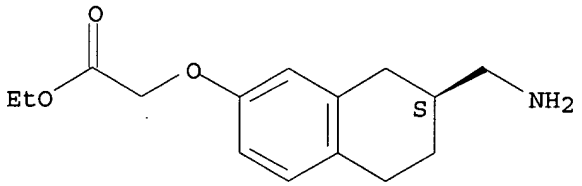
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 8 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-72-3** REGISTRY

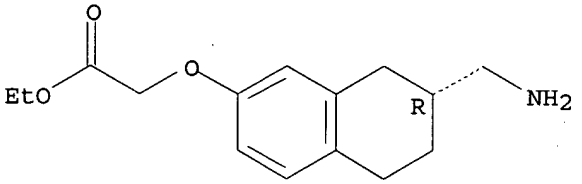
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

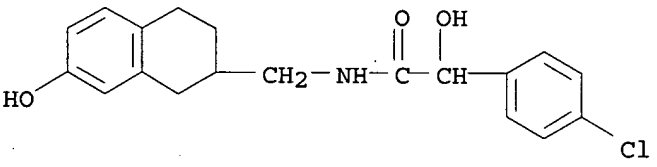
L11 ANSWER 9 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-71-2** REGISTRY

Absolute stereochemistry.



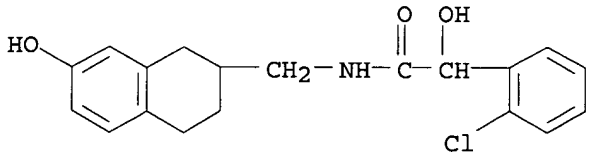
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 10 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-69-8** REGISTRY



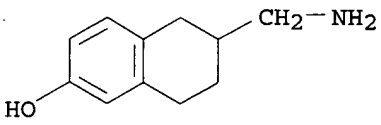
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 11 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-68-7** REGISTRY



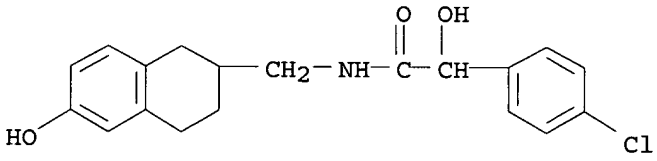
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 12 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-67-6** REGISTRY



● HBr

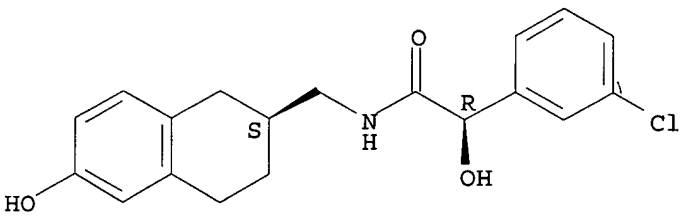
L11 ANSWER 13 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-66-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 14 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-65-4** REGISTRY

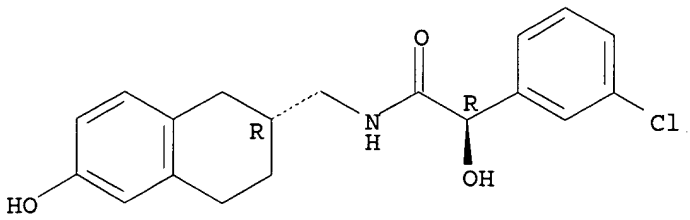
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

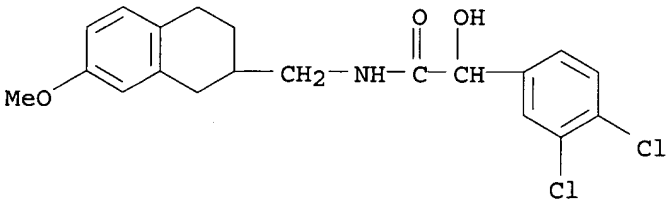
L11 ANSWER 15 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-64-3** REGISTRY

Absolute stereochemistry.



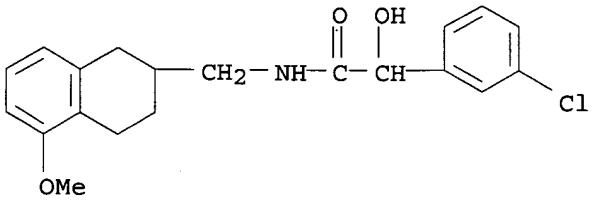
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 16 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-63-2** REGISTRY



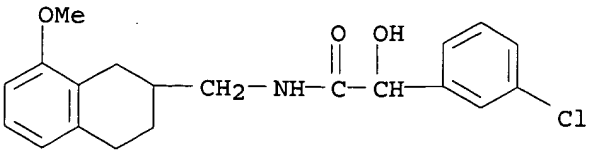
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

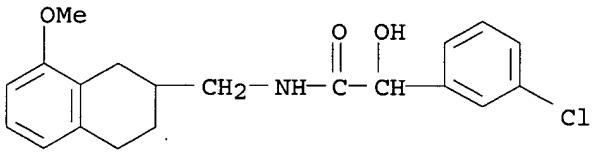
L11 ANSWER 17 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-62-1** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

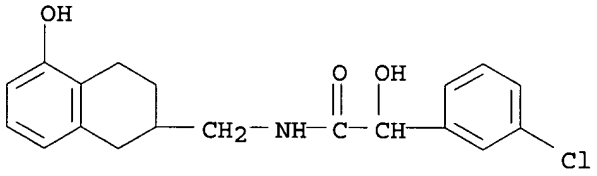
L11 ANSWER 18 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-61-0** REGISTRY





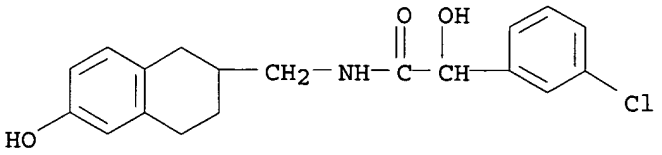
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 19 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-60-9** REGISTRY



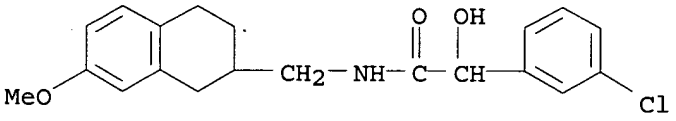
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 20 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-59-6** REGISTRY



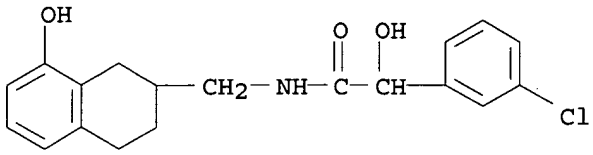
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 21 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-58-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

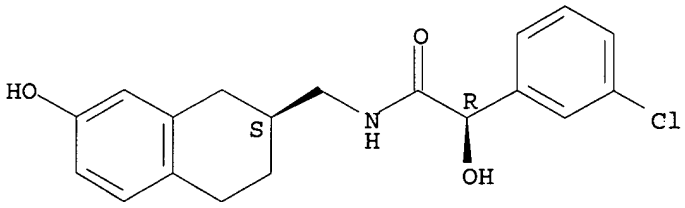
L11 ANSWER 22 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-57-4** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 23 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-56-3** REGISTRY

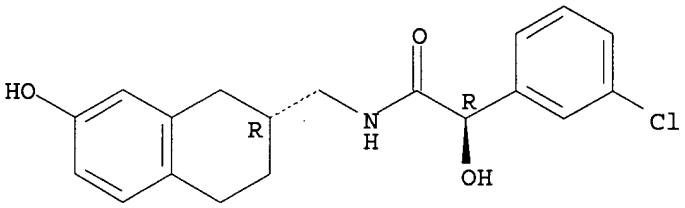
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 24 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-55-2** REGISTRY

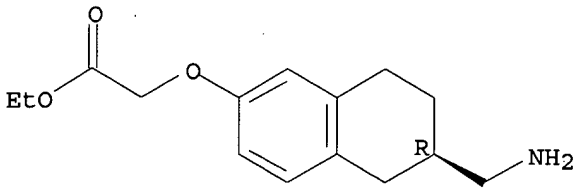
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 25 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-54-1** REGISTRY

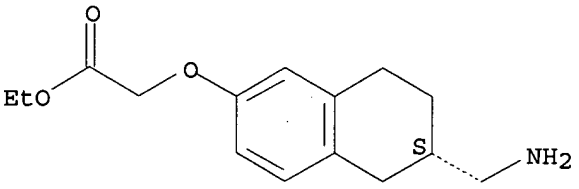
Absolute stereochemistry.



● HCl

L11 ANSWER 26 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-53-0** REGISTRY

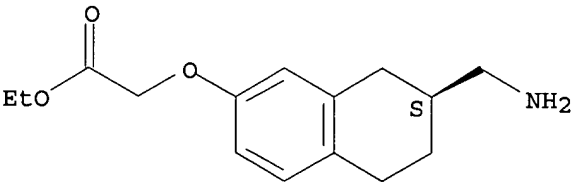
Absolute stereochemistry.



● HCl

L11 ANSWER 27 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-52-9** REGISTRY

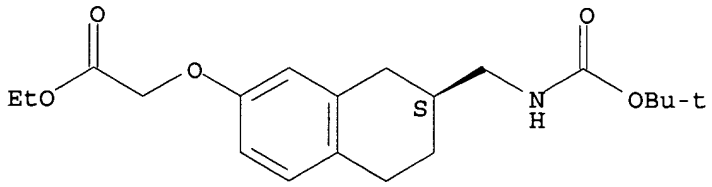
Absolute stereochemistry.



● HCl

L11 ANSWER 28 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-51-8** REGISTRY

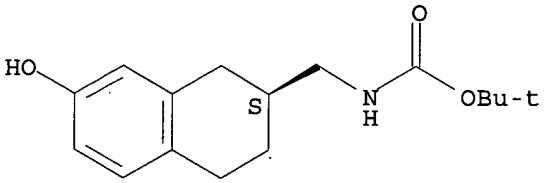
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 29 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-50-7** REGISTRY

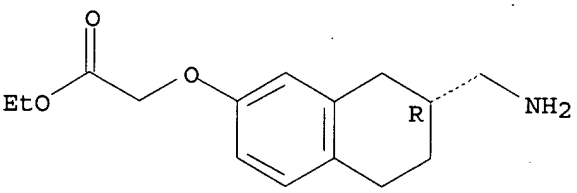
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 30 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-49-4** REGISTRY

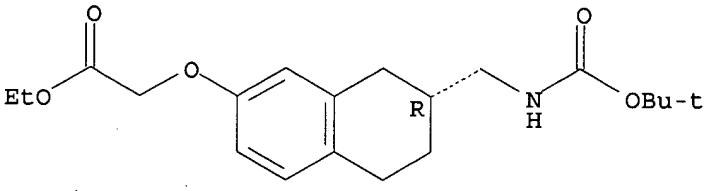
Absolute stereochemistry.

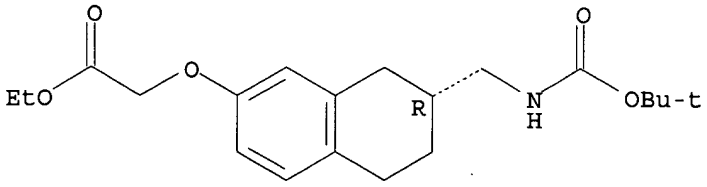


● HCl

L11 ANSWER 31 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-48-3** REGISTRY

Absolute stereochemistry.

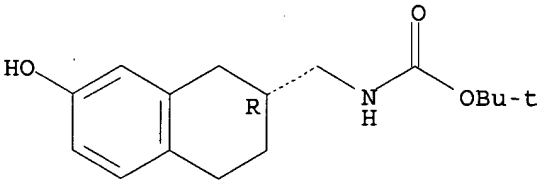




PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 32 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-47-2** REGISTRY

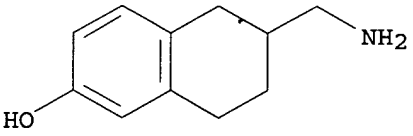
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 33 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-46-1** REGISTRY

Rotation (-).

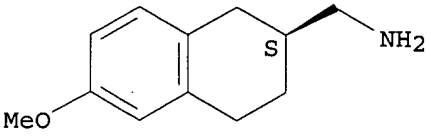


● HBr

L11 ANSWER 34 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-45-0** REGISTRY

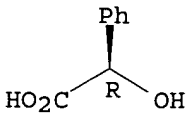
CM 1

Absolute stereochemistry.



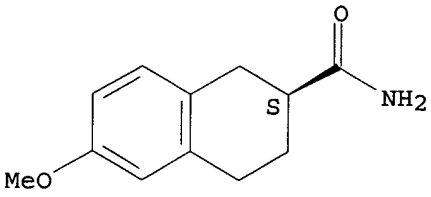
CM 2

Absolute stereochemistry. Rotation (-).



L11 ANSWER 35 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-43-8** REGISTRY

Absolute stereochemistry.

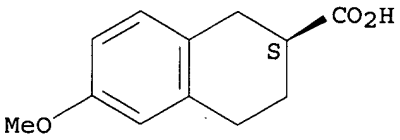


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 36 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-42-7** REGISTRY

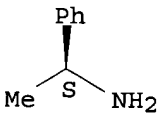
CM 1

Absolute stereochemistry.



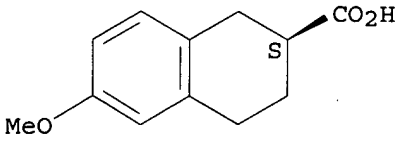
CM 2

Absolute stereochemistry.



L11 ANSWER 37 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-41-6** REGISTRY

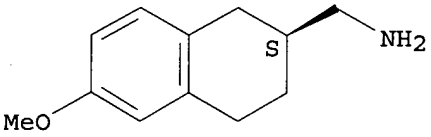
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 38 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-40-5** REGISTRY

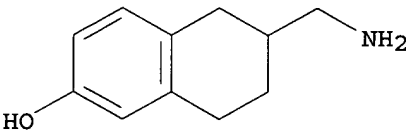
Absolute stereochemistry.



● HCl

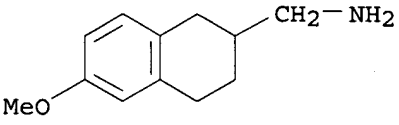
L11 ANSWER 39 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-39-2** REGISTRY

Rotation (+).



● HBr

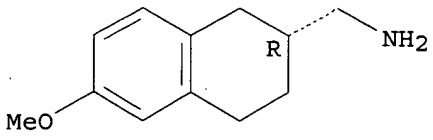
L11 ANSWER 40 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-38-1** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 41 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-37-0** REGISTRY

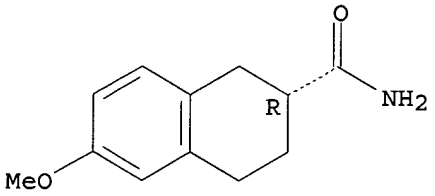
Absolute stereochemistry.



● HCl

L11 ANSWER 42 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-36-9** REGISTRY

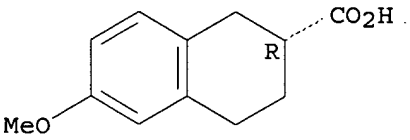
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

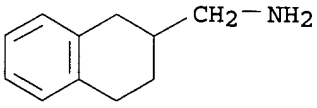
L11 ANSWER 43 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-35-8** REGISTRY

Absolute stereochemistry.



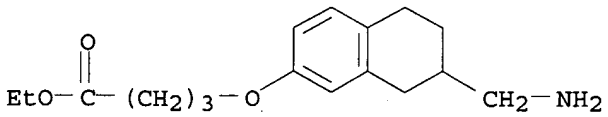
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 44 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-34-7** REGISTRY



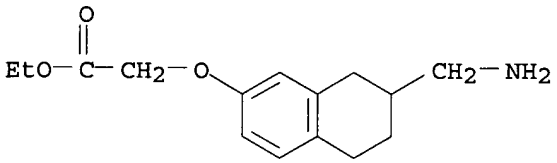
HCl

L11 ANSWER 45 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-33-6** REGISTRY



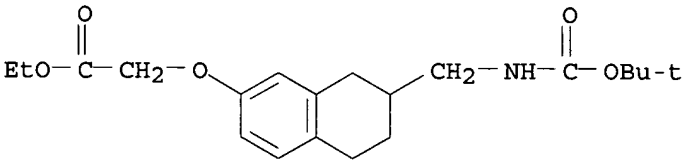
● HCl

L11 ANSWER 46 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-32-5** REGISTRY



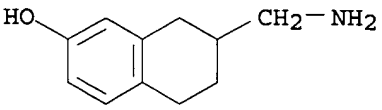
● HCl

L11 ANSWER 47 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-31-4** REGISTRY



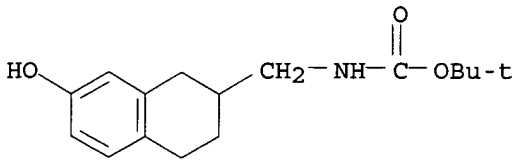
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 48 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-30-3** REGISTRY



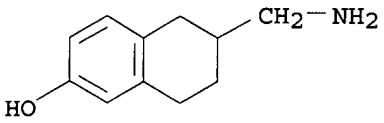
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 49 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-29-0** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

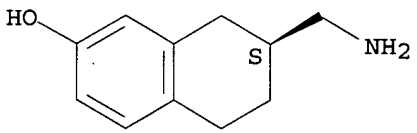
L11 ANSWER 50 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-28-9** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 51 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-27-8** REGISTRY

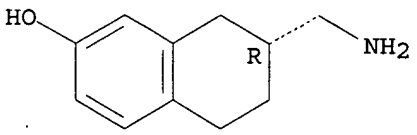
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 52 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-26-7** REGISTRY

Absolute stereochemistry.

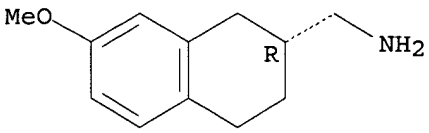


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 53 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-25-6** REGISTRY

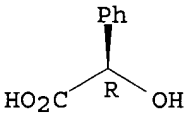
CM 1

Absolute stereochemistry.



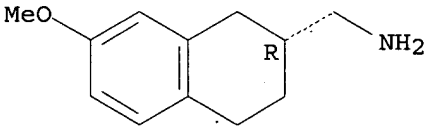
CM 2

Absolute stereochemistry. Rotation (-).



L11 ANSWER 54 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-23-4** REGISTRY

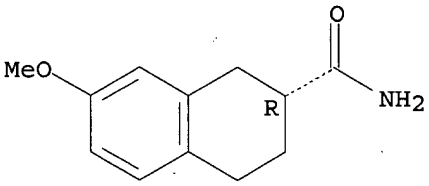
Absolute stereochemistry.



● HCl

L11 ANSWER 55 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-22-3** REGISTRY

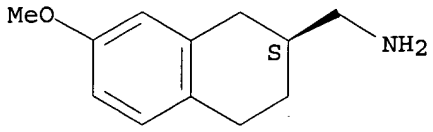
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 56 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-21-2** REGISTRY

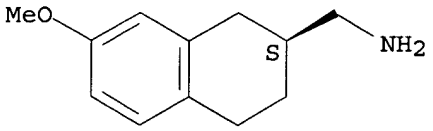
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

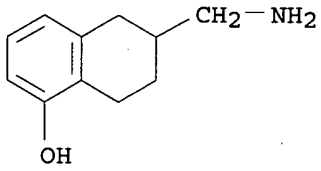
L11 ANSWER 57 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-20-1** REGISTRY

Absolute stereochemistry.



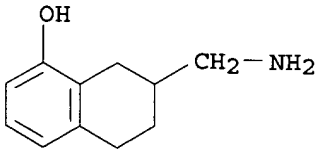
● HCl

L11 ANSWER 58 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-19-8** REGISTRY



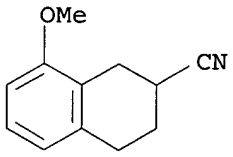
● HBr

L11 ANSWER 59 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-18-7** REGISTRY



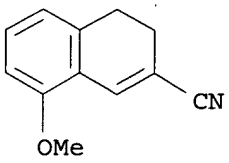
HBr

L11 ANSWER 60 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-17-6** REGISTRY



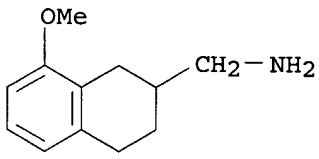
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 61 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-16-5** REGISTRY



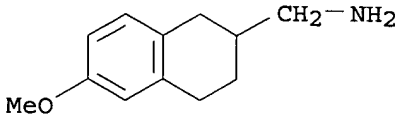
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 62 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-15-4** REGISTRY



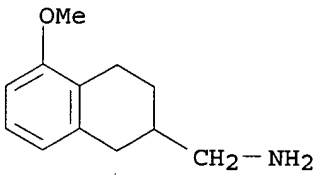
● HCl

L11 ANSWER 63 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-14-3** REGISTRY



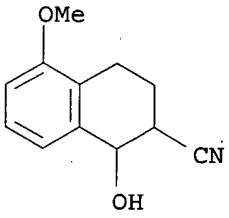
HCl

L11 ANSWER 64 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-13-2** REGISTRY



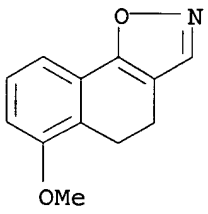
● HCl

L11 ANSWER 65 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-12-1** REGISTRY



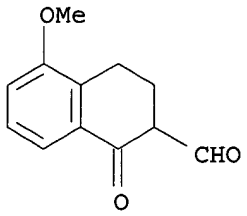
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 66 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-11-0** REGISTRY



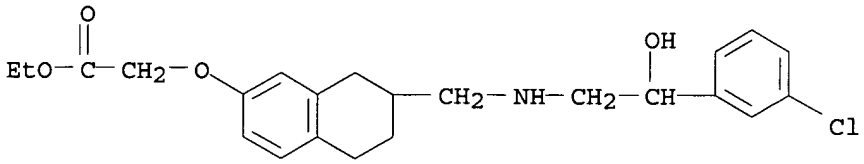
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 67 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-10-9** REGISTRY



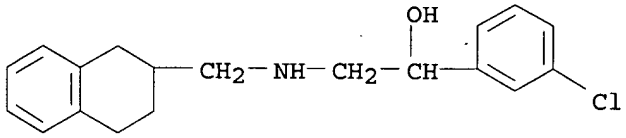
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 68 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-09-6** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

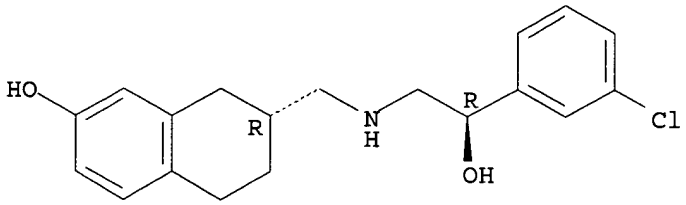
L11 ANSWER 69 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-08-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 70 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-07-4** REGISTRY

Absolute stereochemistry.

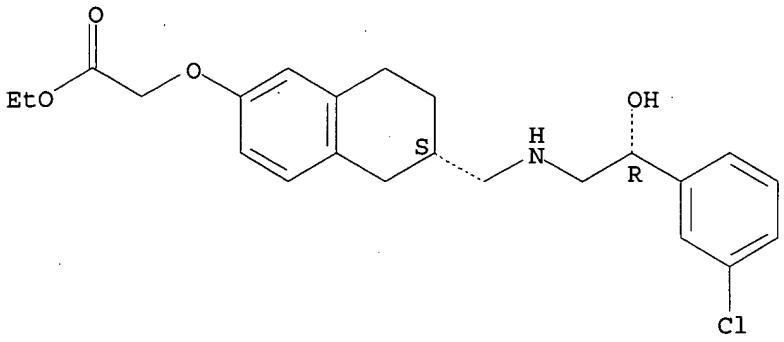


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 71 OF 136 REGISTRY COPYRIGHT 2003 ACS

RN **136759-06-3** REGISTRY

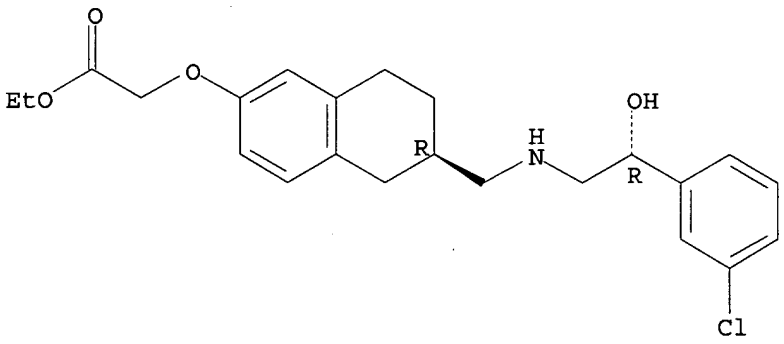
Absolute stereochemistry.



● HCl

L11 ANSWER 72 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-05-2** REGISTRY

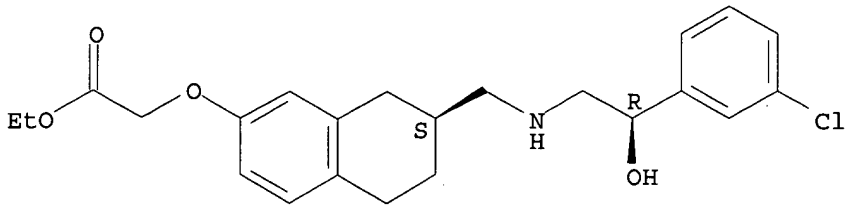
Absolute stereochemistry.



● HCl

L11 ANSWER 73 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-04-1** REGISTRY

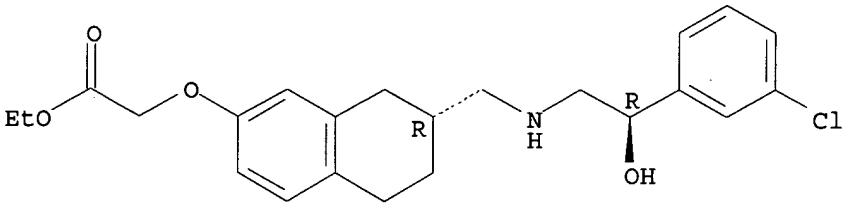
Absolute stereochemistry.



● HCl

L11 ANSWER 74 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-03-0** REGISTRY

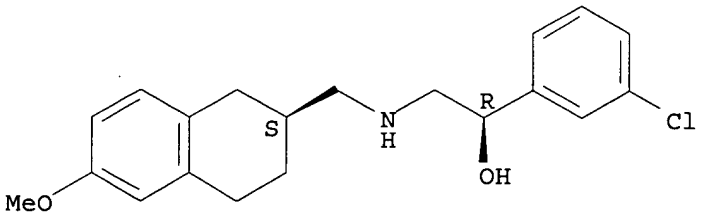
Absolute stereochemistry.



● HCl

L11 ANSWER 75 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-02-9** REGISTRY

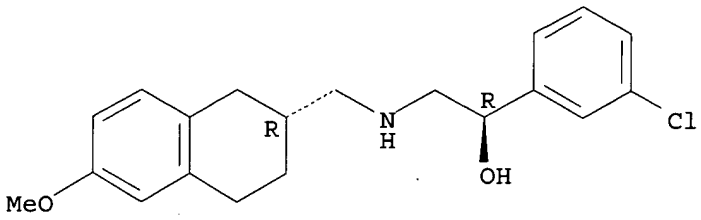
Absolute stereochemistry.



● HCl

L11 ANSWER 76 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-01-8** REGISTRY

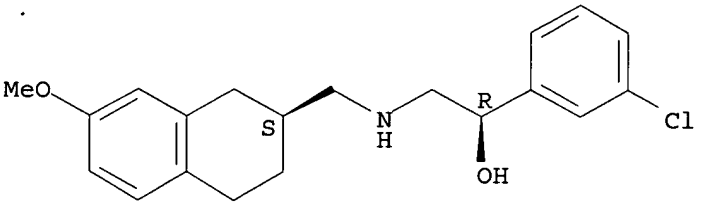
Absolute stereochemistry.



● HCl

L11 ANSWER 77 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136759-00-7** REGISTRY

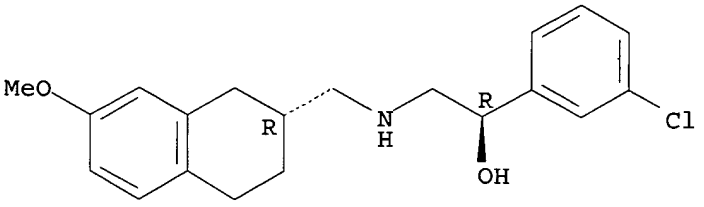
Absolute stereochemistry.



● HCl

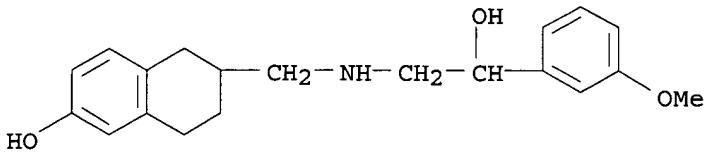
L11 ANSWER 78 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-99-1** REGISTRY

Absolute stereochemistry.



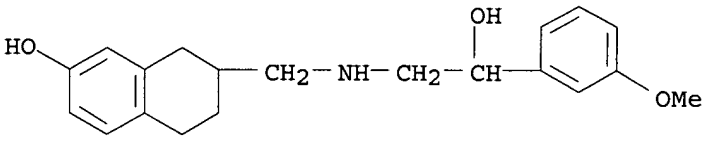
HCl

L11 ANSWER 79 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-98-0** REGISTRY



● HCl

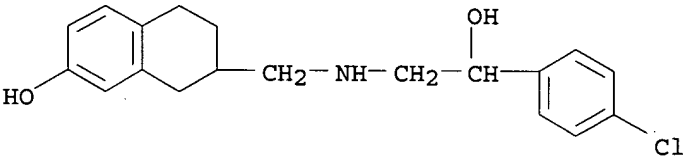
L11 ANSWER 80 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-97-9** REGISTRY



● HCl

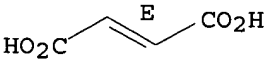
L11 ANSWER 81 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-96-8** REGISTRY

CM 1



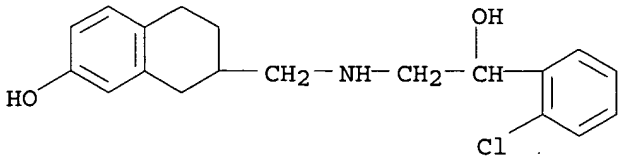
CM 2

Double bond geometry as shown.



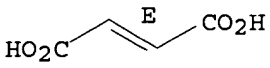
L11 ANSWER 82 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-94-6** REGISTRY

CM 1

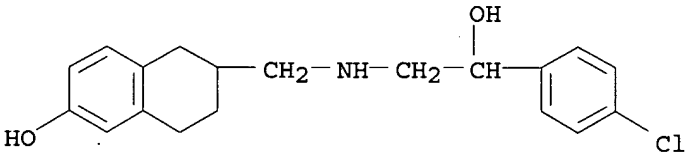


CM 2

Double bond geometry as shown.



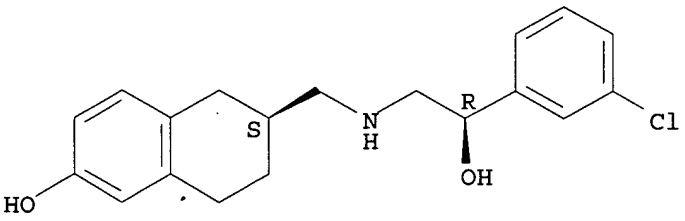
L11 ANSWER 83 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-92-4** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 84 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-91-3** REGISTRY

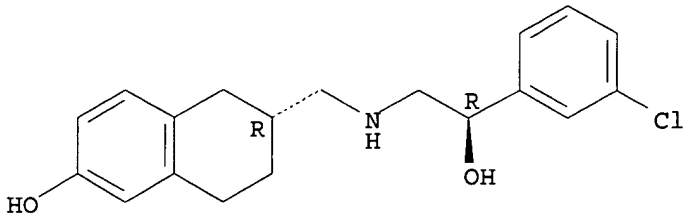
Absolute stereochemistry.



● HCl

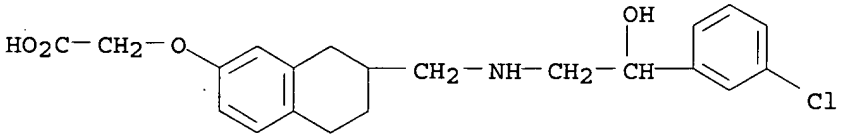
L11 ANSWER 85 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-90-2** REGISTRY

Absolute stereochemistry.



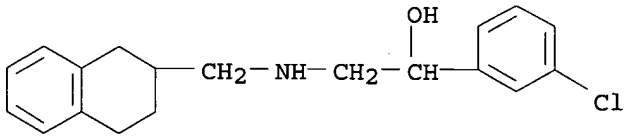
● HCl

L11 ANSWER 86 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-89-9** REGISTRY



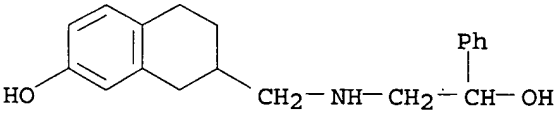
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 87 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-88-8** REGISTRY



● HCl

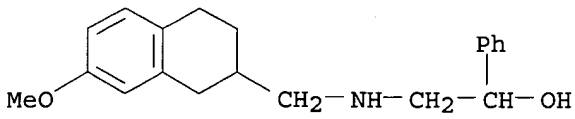
L11 ANSWER 88 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-87-7** REGISTRY



HCl

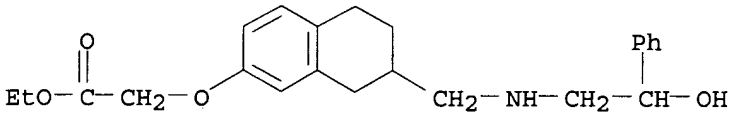
L11 ANSWER 89 OF 136 REGISTRY COPYRIGHT 2003 ACS

RN **136758-86-6** REGISTRY



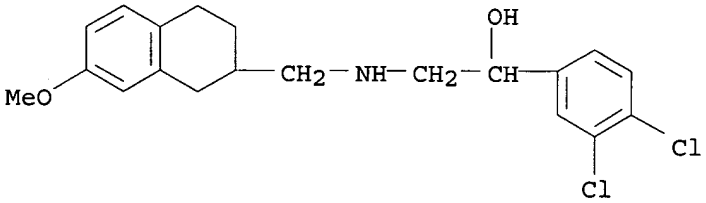
● HCl

L11 ANSWER 90 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-85-5** REGISTRY



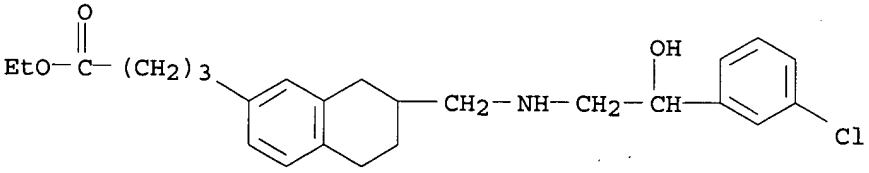
● HCl

L11 ANSWER 91 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-84-4** REGISTRY

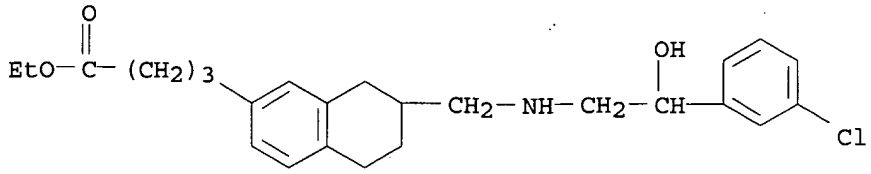


● HCl

L11 ANSWER 92 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-83-3** REGISTRY

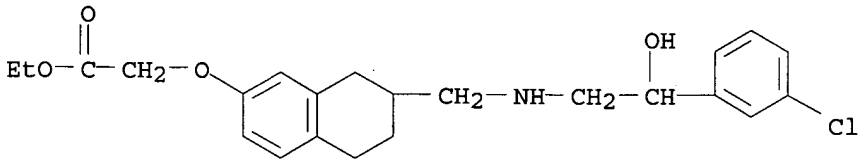


HCl



● HCl

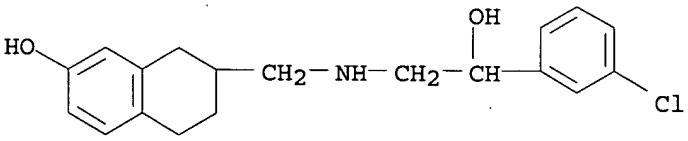
L11 ANSWER 93 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-82-2** REGISTRY



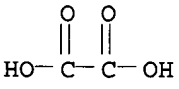
● HCl

L11 ANSWER 94 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-81-1** REGISTRY

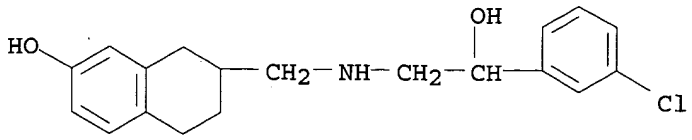
CM 1



CM 2

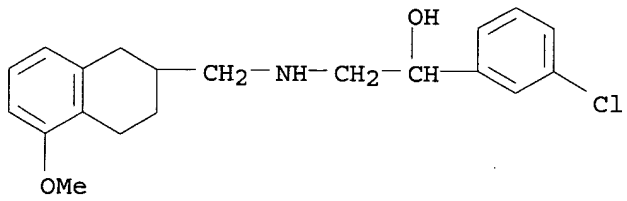


L11 ANSWER 95 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-80-0** REGISTRY



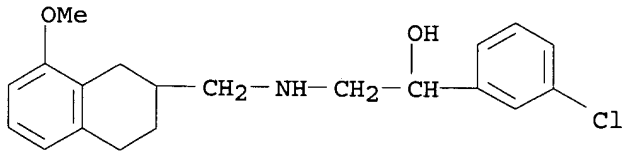
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 96 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-79-7** REGISTRY



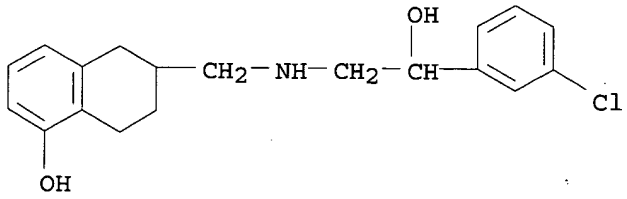
● HCl

L11 ANSWER 97 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-78-6** REGISTRY



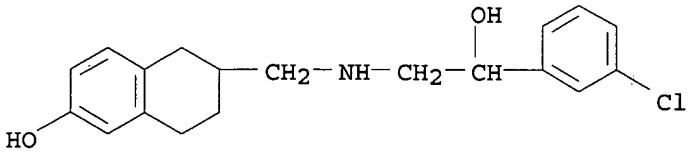
● HCl

L11 ANSWER 98 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-77-5** REGISTRY



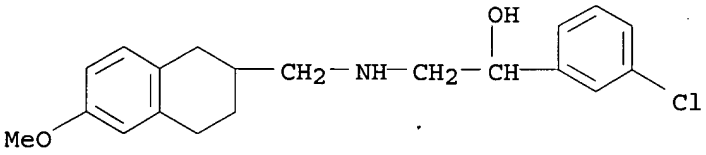
● HCl

L11 ANSWER 99 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-76-4** REGISTRY



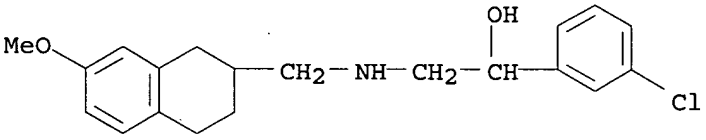
● HCl

L11 ANSWER 100 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-75-3** REGISTRY



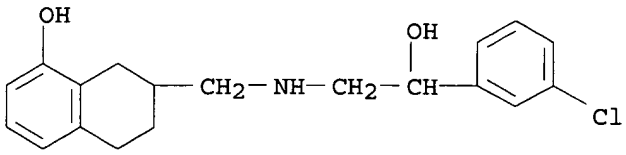
● HCl

L11 ANSWER 101 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-74-2** REGISTRY



● HCl

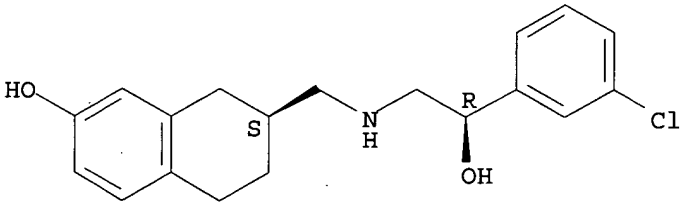
L11 ANSWER 102 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-73-1** REGISTRY



● HCl

L11 ANSWER 103 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-72-0** REGISTRY

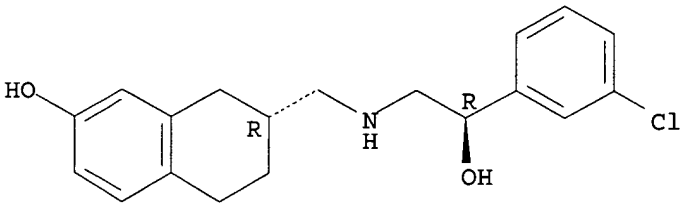
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

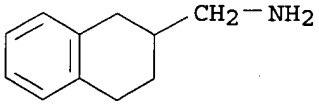
L11 ANSWER 104 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136758-71-9** REGISTRY

Absolute stereochemistry.



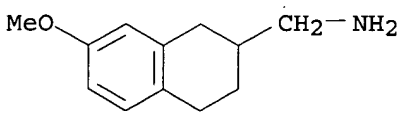
● HCl

L11 ANSWER 105 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **129280-17-7** REGISTRY



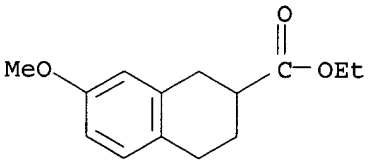
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 106 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **108048-61-9** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

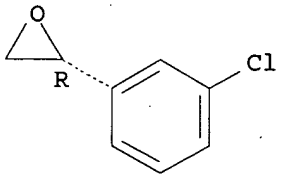
L11 ANSWER 107 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **108048-57-3** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 108 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **62600-71-9** REGISTRY

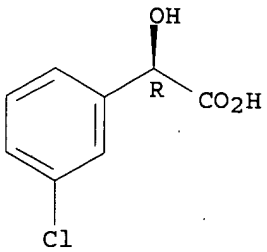
Absolute stereochemistry. Rotation (+).

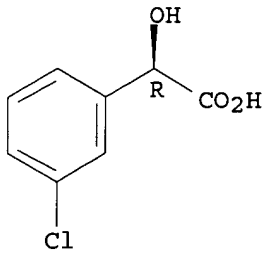


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 109 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **61008-98-8** REGISTRY

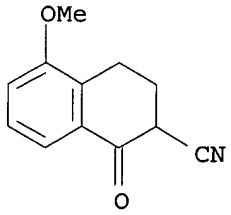
Absolute stereochemistry.





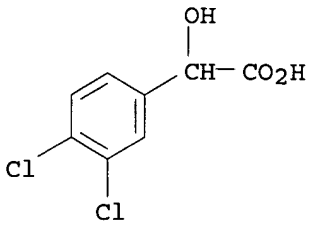
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 110 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **57709-91-8** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

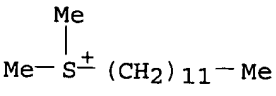
L11 ANSWER 111 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **56071-99-9** REGISTRY



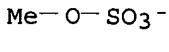
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 112 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **51186-33-5** REGISTRY

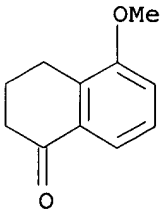
CM 1



CM 2

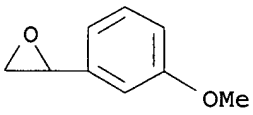


L11 ANSWER 113 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **33892-75-0** REGISTRY



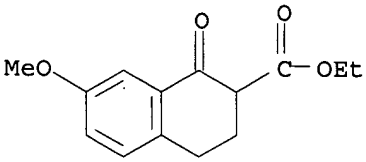
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 114 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **32017-77-9** REGISTRY



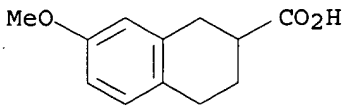
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 115 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **31846-34-1** REGISTRY



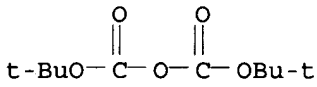
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 116 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **24833-31-6** REGISTRY



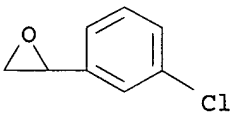
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 117 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **24424-99-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

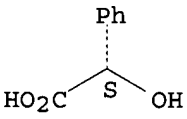
L11 ANSWER 118 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **20697-04-5** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

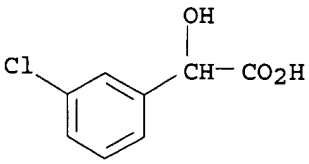
L11 ANSWER 119 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **17199-29-0** REGISTRY

Absolute stereochemistry. Rotation (+).



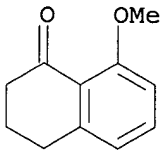
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 120 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **16273-37-3** REGISTRY



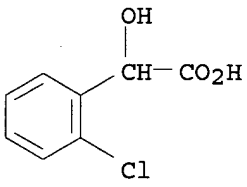
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 121 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **13185-18-7** REGISTRY



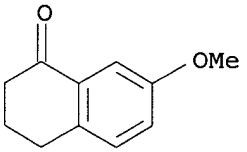
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 122 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **10421-85-9** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

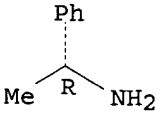
L11 ANSWER 123 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **6836-19-7** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 124 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **3886-69-9** REGISTRY

Absolute stereochemistry.



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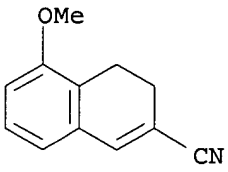
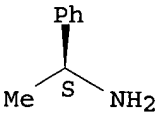
L11 ANSWER 125 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **2825-47-0** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 126 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **2627-86-3** REGISTRY

Absolute stereochemistry.



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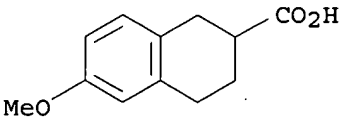
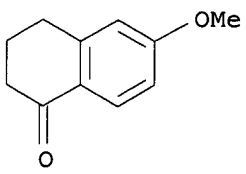
L11 ANSWER 127 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **2471-69-4** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

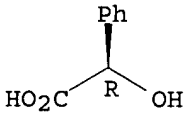
L11 ANSWER 128 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **1078-19-9** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 129 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **611-71-2** REGISTRY

Absolute stereochemistry. Rotation (-).



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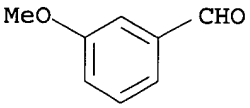
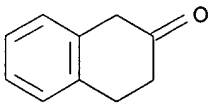
L11 ANSWER 130 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **591-31-1** REGISTRY



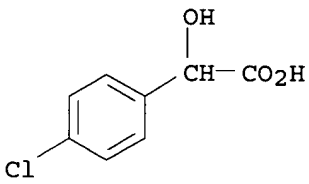
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 131 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **530-93-8** REGISTRY



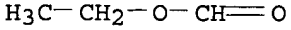
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 132 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **492-86-4** REGISTRY



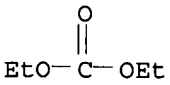
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 133 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **109-94-4** REGISTRY



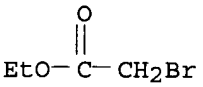
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 134 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **105-58-8** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L11 ANSWER 135 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **105-36-2** REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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L11 ANSWER 1 OF 136 REGISTRY COPYRIGHT 2003 ACS
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RN **136781-73-2** REGISTRY

L11 ANSWER 3 OF 136 REGISTRY COPYRIGHT 2003 ACS
RN **136781-72-1** REGISTRY

L11 ANSWER 4 OF 136 REGISTRY COPYRIGHT 2003 ACS
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L11 ANSWER 5 OF 136 REGISTRY COPYRIGHT 2003 ACS
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RN **96-09-3** REGISTRY

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